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Study protocol to assess the effectiveness and safety of a flexible family visitation model in adult intensive care units: a cluster-randomized, crossover trial (ICU VISITS STUDY)

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Keywords:	delirium, family, health personnel, critical care, intensive care unit

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Study protocol to assess the effectiveness and safety of a flexible family visitation model in adult intensive care units: a cluster-randomized, crossover trial (ICU VISITS STUDY)

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ABSTRACT

Introduction: Flexible intensive care unit (ICU) visiting hours have been proposed as a means to improve patient- and family-centered care. However, randomized trials evaluating the effects of flexible family visitation models (FFVMs) are scarce. This study aims to compare the effectiveness and safety of an FFVM versus a restrictive family visitation model (RFVM) on delirium prevention among ICU patients, as well as to analyze its potential effects on family members and ICU professionals.

Methods and analysis: A cluster-randomized crossover trial involving adult ICU patients, family members, and ICU professionals will be conducted. Forty medical-surgical Brazilian ICUs with RFVMs (<4.5 h/day) will be randomly assigned to either an RFVM (visits according to local policies) or an FFVM (visitation during 12 consecutive hours per day) group at a 1:1 ratio. After enrollment and follow-up of 25 patients, each ICU will be switched over to the other visitation model, until 25 more patients per site are enrolled and followed. The primary outcome will be the cumulative incidence of delirium among ICU patients, measured twice a day using the Confusion Assessment Method for the ICU. Secondary outcome measures will include delirium-free days, ventilator-free days, any ICU-acquired infections, ICU length of stay, and all-cause hospital mortality among the patients; symptoms of anxiety and depression and satisfaction among the family members; and prevalence of symptoms of burnout among the ICU professionals. Tertiary outcomes will include need for antipsychotic agents and/or mechanical restraints, unplanned loss of invasive devices, and ICU-acquired pneumonia, urinary tract infection, or bloodstream infection among the patients; self-perception of involvement in patient care among the family members; and satisfaction among the ICU professionals.

Ethics and dissemination: The study protocol has been approved by the research ethics committee of all participant institutions. We aim to disseminate the findings through international conferences and peer-reviewed journals.

Trial registration: ClinicalTrials.gov, NCT02932358, Registered 11 October 2016.

Keywords: delirium, family, health personnel, critical care, intensive care unit

Strengths and limitations of this study:

- The present study is the first large-scale trial aimed to evaluate the effects of different ICU visiting policies on relevant outcomes among patients, family members and ICU professionals.
- This study is designed as a cluster-randomized crossover trial, which reduces the risk of contamination and improves covariate balance between the two study arms and statistical efficiency.
- This study uses strategies to enhance the implementation and evaluation of complex interventions such as some degree of adaptability to local circumstances, a learning period to study interventions, and assessment of fidelity and quality of the implementations.
- The results of this study will allow health care professionals, researchers, and policymakers to draw conclusions about the efficacy and safety of a flexible family visitation model in adult ICUs.

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LIST OF ABBREVIATIONS

APACHE-II	Acute Physiology and Chronic Health Evaluation II
BRICNet	Brazilian Research in Intensive Care Network
CAM-ICU	Confusion Assessment Method for the ICU
CCFNI	Critical Care Family Needs Inventory
FFVM	Flexible Family Visitation Model
HADS	Hospital Anxiety and Depression Scale
ICC	Intraclass Correlation Coefficient
ICU	Intensive Care Unit
MBI	Maslach Burnout Inventory
PRE-DELIRIC	PREdiction of DELIRium in ICU patients
RASS	Richmond Agitation Sedation Scale
RFVM	Restrictive Familiar Visitation Model
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials

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INTRODUCTION

Adult intensive care unit (ICU) visitation policies vary worldwide; generally, patients admitted to the ICU are only allowed visitors during certain periods of the day.[1-3] Congruent with this scenario, most Brazilian ICUs have a restrictive policy of family visits in which visiting hours typically last from 30 min to 1 h, two to three times a day.[4] These restrictive ICU-visit policies are rooted mainly in a theoretical increased risk of physiological stress, infectious complications, and disorganization of care.[5] However, these theoretical risks have not been consistently confirmed by the scarce literature on this subject,[6-9] and flexible ICU visiting hours have been proposed as a means to improve outcomes through patient- and family-centered care and delirium prevention.[10-12]

Evidence from small observational and before-and-after studies suggests that flexible ICU visitation policies are associated with higher satisfaction among patients and patients' families and with reduction of patient stress.[13, 14] Accordingly, one pilot randomized trial showed reduction in cardiocirculatory complications among ICU patients admitted during periods of unrestricted visiting hours, possibly due to reduction of anxiety and establishment of a more favorable hormonal profile.[6] Moreover, some studies suggest the potential role of presence of family members as a strategy to prevent ICU delirium.[15-17] One small prospective single-center before-and-after study found a reduction of 50% in the cumulative incidence of delirium by changing the visitation policy from a restrictive model (4.5 h/day) to an extended model (12 h/day); the length of delirium and ICU stay was also reduced in this study.[12] In this regard, the presence of family in the critical care setting is suggested as a means to achieve better pain control, reduce the use of sedatives, and participate in the re-orientation and cognitive stimulation of patients. These benefits have been associated with lower incidence of

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delirium in studies evaluating multicomponent non-pharmacological interventions to prevent delirium, and constitute the rationale for the F (Family Engagement and Empowerment) component of the ABCDEF bundle, an evidence-based approach to prevent delirium.[18-21]

Regarding possible risks associated with flexible ICU-visit policies, some studies have shown that ICU professionals sometimes perceive visits as a source of increased workload and disorganization in patient care, instead of considering families as 'one' with the patient and as potential sources of reassurance and comfort.[22-23] In a single center study,[23] 59% of ICU staff members stated that the open visitation policy impaired the organization of patient care, and 72% believed that their work suffered more interruptions due to the extended presence of families in the ICU. Congruent with these data, one before-and-after study with 9 ICUs [24] showed a significant increase in burnout levels among ICU professionals after a partial liberalization of visiting policies. The impact of educational strategies directed to ICU visitors in the context of flexible family visitation policies to prevent disorganization of patient care and burnout among ICU professionals is not known. In relation to the risk of infection, this topic has been evaluated by few underpowered studies.[12, 15, 25] Although one study [15] showed greater environmental microbial contamination during an open policy of ICU visitation, published studies [12, 15, 25] failed to show an association between flexible ICU visiting hours and nosocomial infection. Lastly, the impact of flexible ICU visiting hours on symptoms of anxiety and depression of family members is not well studied: there is plausibility for decreased anxiety and depression with flexible ICU visiting hours as a result of improved access to information and more effective sharing of the decision-making process;[26] conversely, it is also plausible to assume that anxiety and depression will increase as a result of higher exposure of family

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members to complex situations such as terminality and the patient's emotional and physical suffering.[27, 28]

The implementation of a flexible family ICU-visitation policy, although promising due to its low-cost and potential to improve quality of care, is a complex organizational process, given that multiple populations involved in this context may be affected by the intervention in different ways. Additionally, most evidence regarding this intervention is originated from underpowered observational and before-and-after studies. Specifically, no large-scale randomized trial so far has evaluated the potential impact of different ICU visitation models on patient, family, and ICU staff outcomes. We hypothesize that compared to the restrictive family visitation model (RFVM), a flexible family visitation model (FFVM) supported by visitor education will reduce the cumulative incidence of delirium among adult ICU patients, reduce symptoms of anxiety and depression, and increase satisfaction with care among family members without increasing burnout levels among ICU professionals.

OBJECTIVES

Primary objective

The aim of the present study is to assess if an FFVM, compared to an RFVM, can prevent delirium in adult ICU patients.

Secondary objectives

Our secondary objective is to compare the efficacy and safety of both ICU visitation models with regard to three sets of variables: ICU/patient related variables (delirium-free days, ventilator-free days, ICU-acquired infections, ICU length of stay, all-cause hospital mortality, need for antipsychotic use, need for mechanical restraints,

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and unplanned loss of invasive devices), family-related variables (symptoms of anxiety and depression, satisfaction, and self-perception of involvement in patient care), and ICU staff variables (prevalence of symptoms of burnout syndrome and satisfaction).

METHODS

The present study protocol follows the SPIRIT statement recommendations.[29] The items from the World Health Organization trial registration data set are described in Supplementary File 1. This study protocol was registered at clinicaltrials.gov before the randomization of the first cluster (NCT02932358).

Study design

The present study was designed to be a cluster-randomized, crossover trial involving mixed medical-surgical ICUs. In this study, the unit of randomization is the ICU, since the proposed intervention involves components at the organizational level and is intended to be implemented in the whole ICU and not for selected patients. All ICUs will receive both FFVM and RFVM, and the randomization will determine in which order the visitation models will be evaluated in each ICU (Figure 1). The initial intervention (phase 1) will involve ICU randomization to either an FFVM or an RFVM. In phase 2, each ICU will be crossed over to the other visitation model. The study analysis will be performed at the subject level according to the intention-to-treat principle and accounts for the cluster-randomized crossover design.

Participants

Cluster eligibility, recruitment, and exclusion criteria

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Brazilian adult ICUs of public and philanthropic hospitals will be invited to participate in the trial. Mixed medical-surgical ICUs with at least 6 beds and a restrictive policy of family visitation (<4.5 h/day) are considered eligible. ICUs with structural or organizational impediments to flexible family visitation, according to the Brazilian resolution of minimal operational requirements for ICUs,[30] will be excluded.

Patient eligibility, recruitment, and exclusion criteria

Consecutive patients aged ≥18 years admitted to the ICU during phases 1 and 2 will be enrolled in each cluster. Subjects in a coma (Richmond Agitation Sedation Scale [RASS] [31] -4 or -5) lasting >96 h from the moment of first evaluation for recruitment, and those with delirium at baseline (positive Confusion Assessment Method for ICU [CAM-ICU] [32]) will be excluded. The following exclusion criteria will also be applied: cerebral death, aphasia, severe hearing deficit, predicted ICU length of stay <48 h, exclusive palliative treatment at ICU admission, unavailability of a family member to participate in the flexible family visits, unlikelihood to survive >24 h, prisoner status, and lastly, readmission to the ICU after enrolment in the study.

Family member eligibility, recruitment, and exclusion criteria

The sample of family members will include one family member per patient enrolled into the study, with the closest family member being selected. Family members who do not speak Portuguese or have serious impediment in answering the self-applied questionnaires (e.g., illiteracy or severe visual or hearing limitations) will be excluded.

ICU professionals' eligibility, recruitment, and exclusion criteria

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All bedside ICU professionals (physicians, nurses, nursing technicians, and physiotherapists) of each cluster who assist patients during the daytime for at least 20 h per week will be enrolled. ICU professionals who have a planned leave of absence of >15 days during phase 1 will be excluded.

Interventions

The proposed study interventions may be classified as complex because:[33] (a) there is a large number of interacting components within the experimental and control interventions (e.g., changes in ICU processes, education of family members, and engagement and training of the ICU multidisciplinary team); (b) there are several groups targeted by the intervention (ICU patients, family members and ICU professionals); (c) there is a large number and high variability of outcomes (evaluation of different outcome domains in three different target populations); (d) a limited degree of flexibility in the intervention is allowed (educational components may be tailored considering the educational level of the target population, visit hours may be customized according to internal processes of the ICU and expected acceptability of the target population).

We tested the feasibility and acceptability of implementation of the intervention in a single center before-and-after study.[12] Table 1 shows the ICU the components to be implemented during FFVM and RFVM. During both FFVM and RFVM, all visitors will be required to perform hand hygiene by washing their hands with antiseptic soap or using alcohol-based hand-rub formulations, and to wear disposable vests and/or personal protective equipment when appropriate (e.g., contact or droplet precautions). All visitors will receive oral and written guidance about the minimum requirements to promote a safe and restful environment to ICU patients. The

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visitors will be asked to leave the room during some procedures such as intubation, central venous or urinary catheterization, bronchoscopy, electrical cardioversion, and cardiopulmonary resuscitation. As an exception, some patients, during both study interventions, will be allowed to receive visits longer than the maximum limit of visiting hours. This decision will be allowed in the following situations: patient age ≥65 years, terminal illness, and conflicts among patients or family and ICU staff.

Table 1. Components of study interventions

	RFVM	FFVM
Social visits	X	X
Friends and family members allowed (number of simultaneous visitors allowed in patient's room tailored to ICU preferences)		
Max 4.5 hours per day (according to ICU policies prior to randomization)		
Family visits		X
Up to 2 family members allowed (number of simultaneous visitors allowed in patient's room tailored to ICU preferences)		
Maximum of 12 hours per day		
Family members must attend a structured information meeting		
Information meeting		X
For family members who want to participate in the family visits		
Guidance about ICU environment, multidisciplinary work at ICU, common ICU treatments, palliative care, infection control practices, delirium prevention and rehabilitation		
Meeting conducted by a trained healthcare professional that works in the ICU (at least 3x/week)		

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	RFVM	FFVM
Both printed and digital material offered by the study coordinator site (tailored for the specific ICU preferences)		
Printed material focused on patient safety during ICU visits	X	X
Brochure with information about what is allowed and what is not allowed in a social visit		
Printed material focused on education about ICU environment, practices and family engagement on patient care		X
Brochure with information about ICU environment, multidisciplinary work at ICU, common ICU treatments, palliative care, infection control practices, delirium prevention, rehabilitation and family engagement on patient care		
Access to a website focused on education about ICU environment, practices and family engagement on patient care		X
Website with information about ICU environment, multidisciplinary work at ICU, common ICU treatments, palliative care, infection control practices, delirium prevention, rehabilitation and family engagement on patient care		

FFVM, flexible family visitation model; RFVM, restrictive family visitation model.

Flexible Family Visitation Model (FFVM)

In the FFVM, two or fewer close family members will be allowed to visit the patient for up to 12 consecutive hours each day. Family members who agree to join the family visits will have to attend a structured meeting at the ICU in which they will receive guidance about the ICU environment, common ICU treatments, rehabilitation and basic infection control practices, multidisciplinary work at the ICU, and information on palliative care and delirium prevention. Additionally, family members will receive an information brochure and be encouraged to access a website

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(www.utivisitas.com.br), both of which are designed to explain, in simple terms, what happens during and after an ICU stay to legitimize emotions and improve cooperation with relatives without increasing the ICU-staff workload. In addition to family visitation, patients in the FFVM will be allowed to receive social visits at specific time intervals (according to the local ICU policies). Social visits will be offered to patient's friends or other family members that did not qualify for family visitation. The number and duration of social visits will be determined by the patient or proxies. Social visitors will not be required to attend the structured meeting.

Restrictive Family Visitation Model (RFVM)

In the RFVM, patients will be allowed visitors according to routine ICU practices, but limited to the maximum of 4.5 h of visitation per day. Visitors will not be required to attend the structured meeting, because this is the standard of care in Brazil. The length of ICU visiting hours will be similar to that of social visits in the FFVM. The number and duration of visits will be determined by the patient or proxies taking into the account the limits of visiting hours dictated by local policies.

Randomization

The randomization unit is the ICU. In hospitals where there is more than one ICU, each ICU will be considered a distinct randomization units as long as the ICU staff are different. If the staff are the same, all ICUs in the hospital will be considered a single unit of randomization. The allocation of the initial intervention (i.e., FFVM or RFVM) will be performed through blocks of different sizes and stratified by number of ICU beds. A randomization list will be generated, and ICUs will be consecutively randomized as per the date of approval by the local Research Ethics Committee. In

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order to guarantee allocation concealment, a statistician will receive an identification code for each unit but will remain blinded to the identity of the ICU. The statistician will then inform the allocation for each unit identification code to the research coordinator. Lastly, the research coordinator will inform the ICUs regarding the group to which they were initially allocated.

Blinding

It is not feasible to blind the researchers, patients, family members or ICU professionals to the study interventions.

Outcomes

Primary outcome

The primary outcome is the cumulative incidence of delirium during the ICU stay. Diagnosis of delirium will be made using the validated Brazilian translation of the CAM-ICU,[34] which will be applied at least once per 12-h shift in patients with RASS ≥-3, by trained ICU professionals. The cumulative incidence of delirium is defined as the presence of delirium (at least one positive CAM-ICU) on at least one 12-h shift during the ICU stay. Before study initiation, all professionals responsible for CAM-ICU assessment will receive training concerning the CAM-ICU. This specific training will be given both during investigator meetings and on-site. Furthermore, inter-rater reliability measurements of the CAM-ICU and RASS will be performed before study initiation to evaluate the quality of assessments, and, if necessary, additional training will be provided. A sensitivity analysis of the primary outcome adjusted for the baseline risk of developing delirium determined by the PREdiction of DELIRium in ICU patients (PRE-DELIRIC) score [35] will be conducted to check the consistency of the

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results. There will be three a *priori* defined subgroup analyses for the primary endpoint: 1) effectiveness of FFVM vs. RFVM in ICUs according to the PRE-DELIRIC score (patients with a predicted risk <25%, 25-50%, 50–75%, and >75%); 2) effectiveness of FFVM vs. RFVM in ICUs according to patient group (medical vs. surgical, and neurocritical vs. non-neurocritical); and (3) effectiveness of FFVM vs. RFVM in ICUs according to Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores (≤15 vs. >15 points). Additional exploratory subgroup analysis will be performed based on the level of patient's exposure to sedation, ICU professional's workload and proportion of private ICU beds.

Secondary outcomes

Secondary outcome measures include delirium-free days, ventilator-free days, any ICU-acquired infections (pneumonia or urinary tract infection or bloodstream infection according to Centers for Disease Control and Prevention guidelines [36-38]), ICU length of stay, and all-cause hospital mortality among patients; symptoms of anxiety and depression measured by the Hospital Anxiety and Depression Scale (HADS) [39] and satisfaction measured by the Critical Care Family Needs Inventory (CCFNI) [40] among family members; and prevalence of symptoms of burnout syndrome measured by the Maslach Burnout Inventory (MBI) [41] among ICU professionals. All cases of ICU-acquired infections will be adjudicated by an infectious disease physician blinded to the study interventions. Family members and ICU professionals will be evaluated through self-administered questionnaires.

Tertiary outcomes

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Tertiary outcomes will include need for antipsychotic agents and/or mechanical restraints, unplanned loss of invasive devices, and ICU-acquired pneumonia, urinary tract infection, or bloodstream infection among ICU patients; self-perception of involvement in patient care among family members; and satisfaction among ICU workers.

Length of ICU intervention, participant recruitment, and timeline, data collection, management, and monitoring

The length of study phases will be determined by the patient recruitment rate. During phase 1, 25 patients per ICU will be enrolled. After enrollment of the 25th patient, a 30-day period without subject recruitment (i.e., washout period) will occur to allow appropriate conclusion of the follow-up of all recruited patients for the study outcomes and to avoid contamination of the two study arms. After this period, each ICU will be crossed over to the other visitation model (phase 2), with enrollment of an additional 25 ICU patients per ICU.

The study flow diagram is showed in Figure 2 and the schedule of enrollment, interventions and assessments is showed in Supplementary File 2. Patients and family members will be recruited during phases 1 and 2. ICU professionals will be evaluated and followed up only during the phase 1 in order to avoid the carry-over effect. Patients will be followed up from study enrollment to hospital discharge or death, or a maximum of 30 days. Family members will be evaluated at two time points: within the first 48 h of patient inclusion into the study (for baseline data) and within 7 days from patient discharge from ICU or death, or a maximum of 30 days (for outcomes assessment). ICU professionals will be evaluated at two time points: 2 weeks before initiation of the first randomized ICU intervention (for baseline data) and during phase 1 (for outcome

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assessment).

Trained research personnel at the local sites will prospectively collect data on printed case report forms that will be entered into an electronic data capture system (REDCap, Vanderbilt University, Tennessee, USA).[42] In order to allow intention-to-treat analyses, data will be collected and analyzed independent of adherence to study interventions. We will deploy the following procedures to enhance the implementation of study interventions and ensure data quality:

1. All local principal investigators and sub investigators will attend an on-site training session before the beginning of the study to standardize procedures including data collection.
2. All ICUs will have a learning period within the first 15 days of phases 1 and 2. During this period, ICUs will receive the intervention (FFVM or RFVM) but will not recruit subjects. Local investigators will use this period to adapt the ICU staff to the organizational aspects of study intervention, including rules about visiting hours (for both FFVM and RFVM periods), guidance to visitors about the minimum requirements to promote a safe and restful environment to ICU patients (for both FFVM and RFVM periods), role of ICU professionals during family visiting hours (for FFVM period), and conduction of family-members-directed structured meetings (for FFVM period). Furthermore, local investigators will use this period to test the study measurements (CAM-ICU, HADS, CCFNI, MBI) and address concerns regarding case-report filling.
3. The investigators will be able to contact the Coordinating Center to solve any potential issues or problems.
4. Data cleaning will be applied continuously to identify inconsistencies and

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missing data. The centers will be notified of any inconsistencies and missing data and prompted to solve them.

5. The Coordinating Center will review detailed reports on screening, inclusion, follow-up, and data consistency and completeness on a weekly basis. The Coordinating Center will take immediate action to solve any problems.
6. Centers will be monitored throughout the study. On-site monitoring visits will occur during phases 1 and 2. A trained professional appointed by the Coordinating Center will perform the monitoring visit. During the monitoring visits, all information will be considered strictly confidential.

To assess the fidelity and quality of the proposed interventions, we will perform on-site monitoring visits, with a standardized checklist, in order to evaluate if the processes are consistent with the intended intervention or if there are important deviation from the proposed protocol; perception of effectiveness and barriers for implementation will be assessed qualitatively, through semi-structured interviews with healthcare professionals involved in the study.[43] In addition, we will collect data related to the length of visits for included patients and study website access. A data monitoring committee is not required as the risk of study interventions causing significant harms is low.

Sample size and sampling

A minimum of 33 ICUs with recruitment rate of 50 patients per ICU (25 patients per study phase) will be needed (total of 1,650 patients) to detect an absolute difference >6.0% in the cumulative incidence of delirium between the two study arms

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(considering an outcome incidence rate of 20.5% in the RFVM), with 80% power, and two-tailed 0.05 alfa. Two levels of intraclass correlation coefficient (ICC) were considered to calculate the sample size: 0.05 for subjects in the same cluster/time period and 0.01 for subjects in the same cluster/different time periods. Estimates of sample size for the primary outcome were made on the basis of the cumulative incidence of delirium found in a single center before-and-after study that evaluated the effect of different policies of family visitation on the incidence of delirium.[12] In order to compensate for potential ICU and patient losses, the present study plans to recruit 40 ICUs.

Statistical analysis

A detailed statistical analysis plan will be prepared before data analysis and is intended to be published or made available online. All analyses will be conducted with the intention-to-treat principle. The comparison of cumulative incidence of delirium will be performed using models for correlated data considering the ICU as a cluster and presented as risk ratios and 95% confidence intervals. The same models will be used for analysis of secondary and tertiary outcomes, i.e., considering the ICU as a cluster and each outcome with its adequate probability distribution. A statistical significance level of 0.05 will be adopted for all statistical comparisons. The R-Development Core Team will be used for analysis.

DISCUSSION AND TRIAL STATUS

Flexible ICU visiting policy of is a complex intervention, with multiple components, targeting different populations with specific outcomes. Figure 3 describes the logic model for the FFVM. Although several outcomes are expected to have a positive impact, we chose incidence of delirium as primary outcome because it

combines a strong potential for causal and direct association and an important clinical impact. Delirium is a highly prevalent ICU complication and is associated with increased mortality, longer ICU and hospital stay, higher cost of care, and long-term cognitive impairment.[44-46] Therefore, identifying interventions that may reduce the risk and burden of delirium in ICU patients is of paramount importance to improve health-care quality. Other important outcomes, such as ICU-acquired infections and length of stay, levels of burnout among ICU professionals, and symptoms of anxiety and depression and satisfaction among family members may have both a direct and indirect relation with the proposed intervention and, therefore, may represent important markers of effectiveness and safety of the proposed intervention. An FFVM rooted in education of family members may reduce the theoretical risk of increase in ICU staff workload, disorganization of care, and ICU-acquired infections. The higher access to information may have a positive effect on family members' satisfaction and interactions with the patients and ICU professionals. Moreover, an FFVM may result in shorter ICU stay, mediated, for instance, by a lower incidence of delirium; additionally, a better understanding of the condition by the family may avoid delays in ICU discharge.

To the best of our knowledge, this will be the first large-scale, multicenter randomized trial evaluating the effects of different policies of ICU visitation on patients, family members and ICU professionals. Results of this study will allow health care professionals, researchers, and police makers to draw conclusions about the efficacy and safety of a flexible family visitation model in adult ICUs.

Our study has some limitations. First, high variability across institutions is expected; although the chosen ICCs may be considered conservative, there are no estimates in the literature for the proposed intervention, which may result in lack of power if the actual ICC is larger than the estimate. Also, no masking of outcome

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assessors may result in measurement bias for delirium; although blinding is not feasible for the proposed intervention, in order to minimize risk of bias we chose validated methods for delirium evaluation and will make efforts in order to standardize data collection. As the number of patients is small for each cluster, the estimate time for data collection for each study phase is from two to three months; this length of time may not be enough to properly assess burnout in healthcare professionals. Finally, our trial is not designed to evaluate long-term outcomes, such as PTSD in patients and family members, as well as microbiological changes in ICU flora due to a higher circulation of individuals from the community. These issues should be assessed in future studies.

The study design and protocol were finalized in March 2016, and the protocol was approved by the Research Ethics Committee in April 2016. All site investigators were required to participate in at least one of two investigator meetings (November 2016 and April 2017). Currently, this study is recruiting subjects in 34 ICUs representative of the Brazilian geopolitical territory (Figure 4). Another 6 ICUs are in the process of preparation for study initiation. We expect that this study will be completed in April 2018.

ETHICS AND DISSEMINATION

Ethics approval and consent to participate

This study will be conducted according to the resolution no. 466/12 of the Brazilian National Health Council (http://bvsms.saude.gov.br/bvs/saudelegis/cns/2013/res0466_12_12_2012.html). The present study protocol version (version 3, from 22 February 2017) has been approved by the Research Ethics Committee of the coordinating site (approval number: CAAE

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11673812.3.1001.0060) and the research ethics committees of all participant institutions. The need for patients' written informed consent was waived in 32 of 34 participating ICUs, because the standard of care encompasses both study interventions. In 2 of 34 ICUs informed consent will be required for patients or proxies. Informed consent will be required for family members and ICU workers in all ICUs. Site investigators will be responsible for obtaining informed consent from study participants. Subject confidentiality will be assured through data anonymization and controlled access to case report forms, electronic data capture system, and datasets. Any breaches of confidentiality, study protocol, or adverse events attributable to this study will be reported to the above research ethics committees.

Dissemination

We hope to make the study findings widely available and plan to disseminate our results in international conferences and peer-reviewed journals. Authors and collaborators will be involved in reviewing drafts of the manuscripts, press releases and any other publication format arising from this study.

FOOTNOTES

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

RGR, CT, and DBS developed the main study intervention (FFVM). RGR, CT and MF developed the original concept of this study. RGR, MF, NB, ABC, FB, LCPA, FRM,

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JIS, JASP, RBM, and CT contributed to study design. RGR, LGL and CT wrote the first draft of the first draft of the paper, and MF, NB, ABC, FB, LCPA, FRM, JIS, JASP, RBM, CCR, RK, RMM, MMSS, DS, NEG, CE, TR, TH, AA, JMMT, MGB, DCB, ILF, VN, HMV, LCC, PADD, RT, SLSB, and AG revised the first draft. The final manuscript was reviewed by all the authors. All authors read and approved the final manuscript.

Composition and role of the steering committee

The steering committee of ICU Visits study consists of RGR, MF, CCR, ABC, FB, LCPA, FRM, JIS, JASP, RBM, NB, and CT. The role of the steering committee in the present trial is to provide oversight of the conduct of the study. Specific responsibilities of the steering committee include overall supervision of the trial progress and reduction of protocol deviations to a minimum.

Role of the coordinating center

The coordination center of this study (Hospital Moinhos de Vento) is responsible for research materials development, data management, monitoring and communication among all sites, and supervision of the conduct of the trial.

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Role of the funder/sponsor

The funding agency approved the study design and participated in the selection of participant ICUs. The funding agency will have no role in study conduction; collection, management, analysis, and interpretation of the data; and preparation of the manuscript. The funding agency will revise the final version of the manuscript before submission for publication.

Competing interests

The authors declare that they have no competing interests.

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For peer review only

REFERENCES

1. Liu V, Read JL, Scruth E, et al. Visitation policies and practices in US ICUs. *Crit Care* 2013;17:R71. doi: 10.1186/cc12677

2. Garrouste-Orgeas M, Vinatier I, Tabah A, et al. Reappraisal of visiting policies and procedures of patient's family information in 188 French ICUs: a report of the Outcomerea Research Group. *Ann Intensive Care* 2016;6:82. doi: 10.1186/s13613-016-0185-x

3. Spreen AE, Schuurmans MJ. Visiting policies in the adult intensive care units: a complete survey of Dutch ICUs. *Intensive Crit Care Nurs* 2011;27:27-30. doi: 10.1016/j.iccn.2010.10.002

4. Ramos FJ, Fumis RR, de Azevedo LC, et al. Intensive care unit visitation policies in Brazil: a multicenter survey. *Rev Bras Ter Intensiva* 2014;26:339-46. doi: 10.5935/0103-507X.20140052

5. Berwick DM, Kotagal M. Restricted visiting hours in ICUs: time to change. *JAMA* 2004;292:736-7. doi: 10.1001/jama.292.6.736

6. Fumagalli S, Boncinelli L, Lo Nostro A, et al. Reduced cardiocirculatory complications with unrestrictive visiting policy in an intensive care unit: results from a pilot, randomized trial. *Circulation* 2006;113:946-52. doi: 10.1161/CIRCULATIONAHA.105.572537

7. Malacarne P, Corini M, Petri D. Health care-associated infections and visiting policy in an intensive care unit. *Am J Infect Control* 2011;39:898-900. doi: 10.1016/j.ajic.2011.02.018

8. Giannini A, Miccinesi G, Prandi E, et al. Partial liberalization of visiting policies and ICU staff: a before-and-after study. *Intensive Care Med* 2013;39:2180-7. doi: 10.1007/s00134-013-3087-5

For peer review only

9. da Silva Ramos FJ, Fumis RR, Azevedo LC, et al. Perceptions of an open visitation policy by intensive care unit workers. *Ann Intensive Care* 2013;3:34. doi: 10.1186/2110-5820-3-34

10. Levy MM, De Backer D. Re-visiting visiting hours. *Intensive Care Med* 2013;39:2223-5. doi: 10.1007/s00134-013-3119-1

11. Giannini A, Garrouste-Orgeas M, Latour JM. What's new in ICU visiting policies: can we continue to keep the doors closed? *Intensive Care Med* 2014;40:730-3. doi: 10.1007/s00134-014-3267-y

12. Rosa RG, Tonietto TF, da Silva DB, et al. Effectiveness and safety of an extended ICU visitation model for delirium prevention: A Before and After Study. *Crit Care Med* 2017;45:1660-7.

13. Chapman DK, Collingridge DS, Mitchell LA, et al. Satisfaction with elimination of all visitation restrictions in a mixed-profile intensive care unit. *Am J Crit Care* 2016;25:46-50. doi: 10.4037/ajcc2016789

14. Gonzalez CE, Carroll DL, Elliott JS, et al. Visiting preferences of patients in the intensive care unit and in a complex care medical unit. *Am J Crit Care* 2004;13:194-8.

15. Eghbali-Babadi M, Shokrollahi N, Mehrabi T. Effect of family-patient communication on the incidence of delirium in hospitalized patients in cardiovascular surgery ICU. *Iran J Nurs Midwifery Res* 2017;22:327-31. doi: 10.4103/1735-9066.212985

16. Van Rompaey B, Elseviers MM, Schuurmans MJ, et al. Risk factors for delirium in intensive care patients: a prospective cohort study. *Crit Care* 2009;13:R77. doi: 10.1186/cc7892

For peer review only

17. Martinez FT, Tobar C, Beddings CI, et al. Preventing delirium in an acute hospital using a non-pharmacological intervention. *Age Ageing* 2012;41:629-34. doi: 10.1093/ageing/afs060

18. Balas MC, Vasilevskis EE, Olsen KM, et al. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Crit Care Med* 2014;42:1024-36. doi: 10.1097/CCM.0000000000000129

19. Trogrlic Z, van der Jagt M, Bakker J, et al. A systematic review of implementation strategies for assessment, prevention, and management of ICU delirium and their effect on clinical outcomes. *Crit Care* 2015;19:157. doi: 10.1186/s13054-015-0886-9

20. Brummel NE, Girard TD. Preventing delirium in the intensive care unit. *Crit Care Clin* 2013;29:51-65. doi: 10.1016/j.ccc.2012.10.007

21. Siddiqi N, Harrison JK, Clegg A, et al. Interventions for preventing delirium in hospitalised non-ICU patients. *Cochrane Database Syst Rev* 2016;3:CD005563. doi: 10.1002/14651858.CD005563.pub3

22. Davidson JE, Aslakson RA, Long AC. Guidelines for family-centered care in the neonatal, pediatric, and adult ICU. *Crit Care Med* 2017; 45(1):103-128. doi: 10.1097/CCM.0000000000002169

23. Ramos FJ, Fumis RR, Azevedo LC, et al. Perceptions of an open visitation policy by intensive care unit workers. *Ann Intensive Care* 2013;3:34. doi: 10.1186/2110-5820-3-34

24. Giannini A, Miccinesi G, Prandi E, et al. Partial liberalization of visiting policies and ICU staff: a before-and-after study. *Intensive Care Med* 2013;39:2180-7. doi: 10.1007/s00134-013-3087-5

For peer review only

679 25. Malacarne P, Corini M, Petri D. Health care-associated infections and visiting
680 policy in an intensive care unit. *Am J Infect Control* 2011;39:898-900. doi:
681 10.1016/j.ajic.2011.02.018
682 26. Lautrette A, Darmon M, Megarbane B, et al. A communication strategy and
683 brochure for relatives of patients dying in the ICU. *N Engl J Med* 2007;356:469-78. doi:
684 10.1056/NEJMoa063446
685 27. Pochard F, Azoulay E, Chevret S, et al. Symptoms of anxiety and depression in
686 family members of intensive care unit patients: ethical hypothesis regarding decision-
687 making capacity. *Crit Care Med* 2001;29:1893-7.
688 28. Rosendahl J, Brunkhorst FM, Jaenichen D, et al. Physical and mental health in
689 patients and spouses after intensive care of severe sepsis: a dyadic perspective on long-
690 term sequelae testing the Actor-Partner Interdependence Model. *Crit Care Med*
691 2013;41:69-75. doi: 10.1097/CCM.0b013e31826766b0
692 29. Chan AW1, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining
693 standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200-7. doi:
694 10.7326/0003-4819-158-3-201302050-00583
695 30. Ministério da Saúde. Agência Nacional de Vigilância Sanitária (Brazil). Resolução
696 nº 7, de 24 fevereiro de 2010. Dispõe sobre os requisitos mínimos para funcionamento
697 de Unidades de Terapia Intensiva e dá outras providências. Brasília (DF): Ministério da
698 Saúde; 2010.
699 http://bvsms.saude.gov.br/bvs/saudelegis/anvisa/2010/res0007_24_02_2010.html.
700 (accessed 27 Nov 2017).
701 31. Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation-Sedation Scale:
702 validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med*
703 2002;166:1338-44. doi: 10.1164/rccm.2107138

For peer review only

32. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med*. 2001;29:1370-9.

33. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008;337:a1655. doi: 10.1136/bmj.a1655

34. Gusmao-Flores D, Salluh JI, dal-Pizzol F, et al. Validity and reliability of the Brazilian-Portuguese version of three tools to diagnose delirium: CAM-ICU, CAM-ICU Flowsheet and ICDSC. *Crit Care* 2011;15:50. doi: 10.1186/cc10198

35. van den Boogaard M, Pickkers P, Slooter AJ, et al. Development and validation of PRE-DELIRIC (PREdiction of DELIRium in ICu patients) delirium prediction model for intensive care patients: observational multicentre study. *BMJ* 2012;344:e420. doi: 10.1136/bmj.e420

36. Centers for Disease Control and Prevention. Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and non-central line-associated Bloodstream Infection). 2017. https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc_clabscurrent.pdf. (accessed 27 Nov 2017).

37. Centers for Disease Control and Prevention. Pneumonia (Ventilator-associated [VAP] and non-ventilator-associated Pneumonia [PNEU]) Event. 2017. https://www.cdc.gov/nhsn/pdfs/pscmanual/6pscvapcurrent.pdf. (accessed 27 Nov 2017).

38. Centers for Disease Control and Prevention. Urinary Tract Infection (Catheter-Associated Urinary Tract Infection [CAUTI] and Non-Catheter-Associated Urinary Tract Infection [UTI]) and Other Urinary System Infection [USI]) Events. 2017.

For peer review only

https://www.cdc.gov/nhsn/pdfs/pscManual/7pscCauticurrent.pdf. (accessed 27 Nov 2017)

39. Botega NJ, Bio MR, Zomignani MA, et al. Mood disorders among medical in-patients: a validation study of the hospital anxiety and depression scale (HAD). *Rev Saude Publica* 1995;29:355-63.

40. Fumis RR, Nishimoto IN, Deheinzelin D. Measuring satisfaction in family members of critically ill cancer patients in Brazil. *Intensive Care Med* 2006;32:124-8. doi: 10.1007/s00134-005-2857-0

41. Campos JA, Maroco J. [Maslach Burnout Inventory - Student Survey: Portugal-Brazil cross-cultural adaptation]. *Rev Saude Publica* 2012;46:816-24.

42. Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377-81. doi: 10.1016/j.jbi.2008.08.010

43. Moore GF, Audrey S, Barker M, et al. Process evaluation of complex interventions: Medical Research Council guidance. *BMJ* 2015;350:h1258. doi: 10.1136/bmj.h1258

44. Reade MC, Finfer S. Sedation and delirium in the intensive care unit. *N Engl J Med* 2014;370:444-54. doi: 10.1056/NEJMra1208705

45. Salluh JI, Soares M, Teles JM, et al. Delirium epidemiology in critical care (DECCA): an international study. *Crit Care* 2010;14:R210. doi: 10.1186/cc9333

46. Salluh JI, Wang H, Schneider EB, et al. Outcome of delirium in critically ill patients: systematic review and meta-analysis. *BMJ* 2015;350:h2538. doi: 10.1136/bmj.h2538

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FIGURE LEGENDS

Figure 1. Study design.

FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model.

During the study, the ICU intervention (FFVM or RFVM) will be applied to all admitted patients apart of meeting inclusion criteria for the study. The length of study phases in each ICU will be determined by the patient recruitment rate (25 patients in phase 1 and 25 patients in phase 2). Patients and family members will be recruited during phases 1 and 2. ICU professionals will be evaluated and followed up only during the phase 1. Following the recruitment of the 25th patient, during phase 1, a 30-day period without subject recruitment will occur to allow appropriate conclusion of the follow-up of all recruited patients for the study outcomes and to avoid contamination of the two study arms.

Figure 2. Study flow diagram.

FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model.

Figure 3. Logic model for flexible ICU-visiting hours.

FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model.

Figure 4. Geographical distribution of participating ICUs.

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SUPPLEMENTARY MATERIAL

Supplementary File 1. Items from the World Health Organization trial registration data set.

Supplementary File 2. Schedule of enrollment, interventions, and assessments.

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* Collaborators cited by study site (Brazilian estate).

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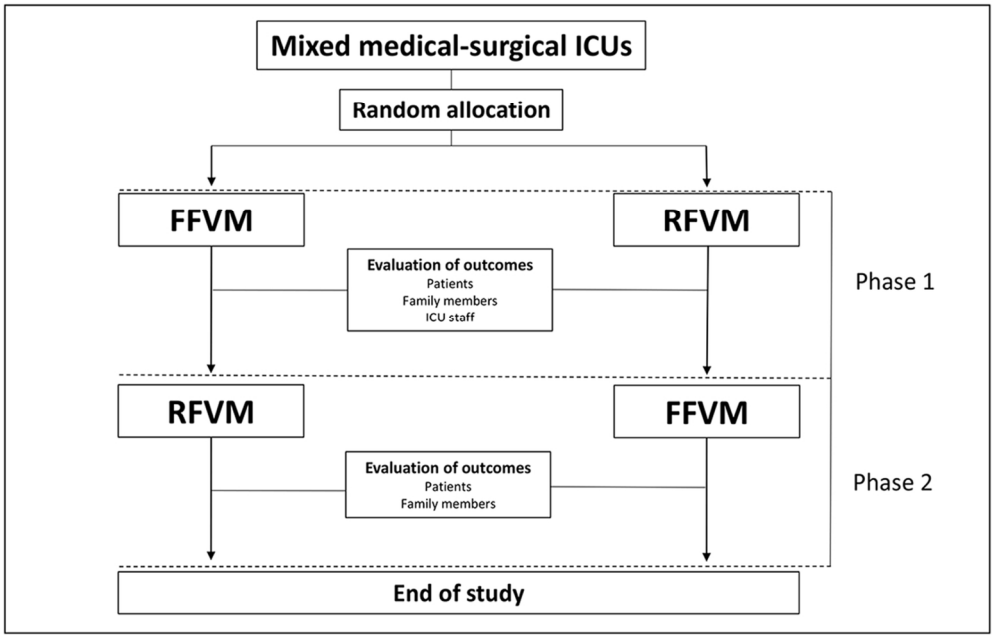

Figure 1. Study design. FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model. During the study, the ICU intervention (FFVM or RFVM) will be applied to all admitted patients apart of meeting inclusion criteria for the study. The length of study phases in each ICU will be determined by the patient recruitment rate (25 patients in phase 1 and 25 patients in phase 2). Patients and family members will be recruited during phases 1 and 2. ICU professionals will be evaluated and followed up only during the phase 1. Following the recruitment of the 25th patient, during phase 1, a 30-day period without subject recruitment will occur to allow appropriate conclusion of the follow-up of all recruited patients for the study outcomes and to avoid contamination of the two study arms.

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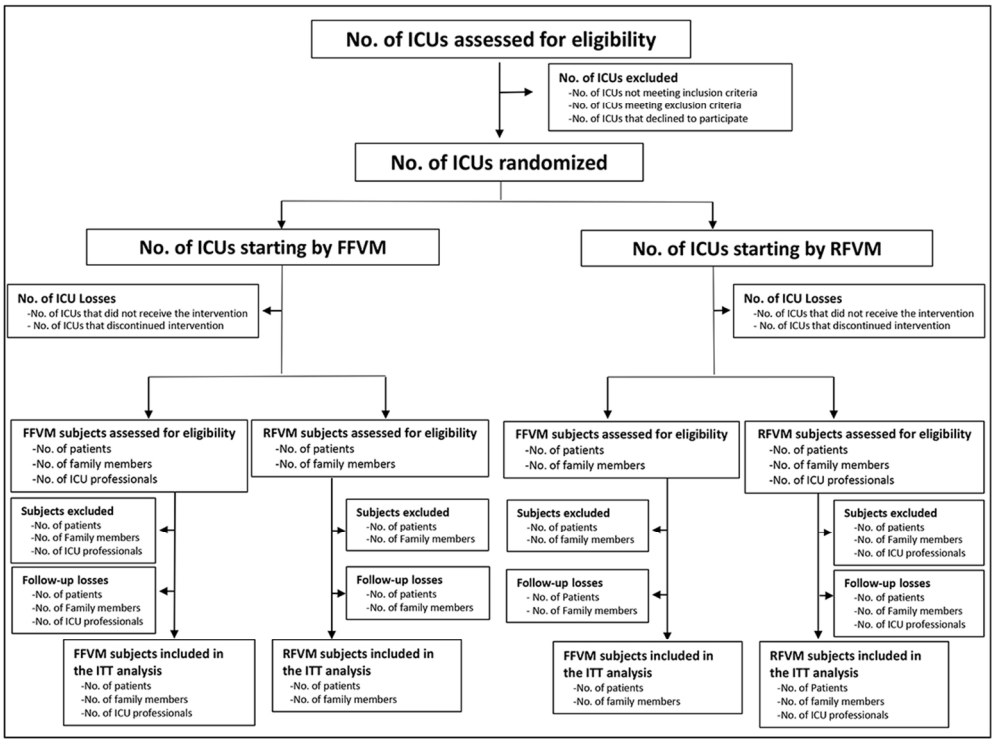

Figure 2. Study flow diagram. FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model.

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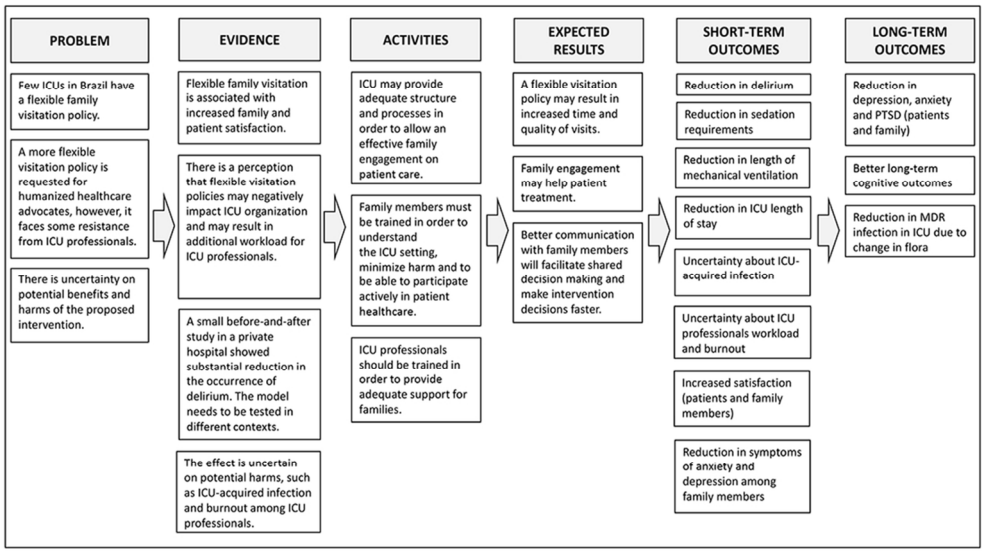

Figure 3. Logic model for flexible ICU-visiting hours. FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model.

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Figure 4. Geographical distribution of participating ICUs.

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Supplementary File 1. Items from the World Health Organization Trial Registration Data Set.

DATA CATEGORY	INFORMATION
Primary registry and trial identifying number	ClinicalTrials.gov NCT02932358
Date of registration in primary registry	11 October 2016
Secondary identifying numbers	CAAE 11673812.3.1001.0060
Source of monetary or material support	The present study was funded by the Brazilian Ministry of Health through the Program of Institutional Development of the Brazilian Unified Health System (PROADI-SUS).
Primary sponsor	Brazilian Ministry of Health
Secondary sponsor	Brazilian Ministry of Health
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Public title	ICU VISITS STUDY
Scientific title	Effectiveness and safety of a flexible family visitation model in adult intensive care units: a cluster-randomized, crossover trial
Countries of recruitment	Brazil
Health conditions or problems studied	Delirium, ICU-acquired infections, anxiety, depression, burnout

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	syndrome.
Interventions	1) Active comparator: Flexible family visitation model – ICU visitation during 12 consecutive hours per day 2) Control comparator: Restrictive family visitation model – ICU visitation according to local policies
Key inclusion and exclusion criteria	1) ICUs - Inclusion criteria: Mixed medical-surgical ICUs with at least 6 beds and a restrictive policy of family visitation (<4.5 h/day) - Exclusion criteria: ICUs with structural or organizational impediments to flexible family visitation. 2) Patients - Inclusion criteria: patients aged ≥18 years admitted to the ICU. - Exclusion criteria: coma lasting > 96hs, cerebral death, aphasia, severe hearing deficit, predicted ICU length of stay <48 h, exclusive palliative treatment at ICU admission, unavailability of a family member to participate in the flexible family visits, unlikelihood to survive >24 h, prisoner status, readmission to the ICU after enrolment in the study. 3) Family members - Inclusion criteria: closest family member of a ICU patient recruited in the study. - Exclusion criteria: family members who do not speak Portuguese or have serious impediment in answering the

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	self-applied questionnaires 4) ICU professionals - Inclusion criteria: ICU bedside professionals (physicians, nurses, nursing technicians, and physiotherapists) who assist patients during the daytime for at least 20 h per week. - Exclusion criteria: professionals who have a planned leave of absence of >15 days during the study.
Study type	Interventional Allocation: randomized Intervention model: crossover assignment Masking: open label Primary purpose: prevention
Date of first enrollment	28 April 2017
Target sample size	1650 patients
Recruitment status	Recruiting
Primary outcome	Cumulative incidence of delirium
Key secondary outcomes	delirium-free days, ventilator-free days, any ICU-acquired infections, ICU length of stay, and all-cause hospital mortality among the patients; symptoms of anxiety and depression and satisfaction among the family members; and prevalence of symptoms of burnout among the ICU professionals.

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Supplementary File 2. Schedule of enrollment, interventions, and assessments.

	Study timeline						
	t1	t2	t3			t4	
	Enrollment of clusters	**Random allocation of clusters**	**Interventions at the cluster level**				
			Phase 1			**Phase 2**	
			Learning curve of phase 1 (15 days)	Recruitment (until the enrollment of the 25th patient)	Period without subject recruitment (30 days)	Learning curve of phase 2 (15 days)	Recruitment (until the enrollment and follow-up of the 50th patient)
ENROLMENT							
Patients				X[1]			X[1]
Family members				X[2]			X[2]
ICU professionals			X				
INTERVENTIONS (cluster level)							
ICUs starting by FFVM							
-FFVM			X	X	X		
-RFVM						X	X
ICUs starting by RFVM							
-FFVM						X	X
-RFVM			X	X	X		
DATA COLLECTION (subjects level)							
Baseline variables							
-Patients				X[1]			X[1]
-Family members				X[2]			X[2]
-ICU professionals			X				
Outcomes							
-Patients				X[3]	X[3]		X[3]
-Family members				X[4]	X[4]		X[4]
-ICU professionals					X		

FFVM, flexible family visitation model; ICU, intensive care unit; RFVM, restrictive family visitation model.

[1] Within the first 48 hours of ICU admission.

[2] Within the first 48hs of patient enrollment.

[3] All patient outcomes will be assessed during the ICU stay, with exception to the hospital mortality, which will be verified at the end of hospitalization.

[4] Within the first 7 days of patient discharge from the ICU.

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SPIRIT
STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: **Study protocol to assess the effectiveness and safety of a flexible family visitation model in adult intensive care units: a cluster-randomized, crossover trial (ICU VISITS STUDY)**

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	7, 12
	2b	All items from the World Health Organization Trial Registration Data Set	Supplemental file 1
Protocol version	3	Date and version identifier	25
Funding	4	Sources and types of financial, material, and other support	27
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1-4, 26, 27
	5b	Name and contact information for the trial sponsor	27
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	28
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	27

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Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	9-11
	6b	Explanation for choice of comparators	9-11
Objectives	7	Specific objectives or hypotheses	11, 12
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	12
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	12, 13
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	12-14
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	14-16
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	15
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	19, 20
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	18-20
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	21,22

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Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	22, 23
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	20-23
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	17, 18
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	18
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	17, 18
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	18
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	18-22
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	12, 18-22

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Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	18-22
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	23
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	23
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	12,22
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	22
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	22
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	22
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	25,26
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	25,26

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Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	26
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	26
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	28
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	26
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	26
	31b	Authorship eligibility guidelines and any intended use of professional writers	26, 27
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	26
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	-
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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BMJ Open

Study protocol to assess the effectiveness and safety of a flexible family visitation model for delirium prevention in adult intensive care units: a cluster-randomized, crossover trial (ICU VISITS STUDY)

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Primary Subject Heading:	Intensive care
Secondary Subject Heading:	Patient-centred medicine
Keywords:	delirium, family, health personnel, critical care, intensive care unit

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Study protocol to assess the effectiveness and safety of a flexible family visitation model for delirium prevention in adult intensive care units: a cluster-randomized, crossover trial (ICU VISITS STUDY)

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ABSTRACT

Introduction: Flexible intensive care unit (ICU) visiting hours have been proposed as a means to improve patient- and family-centered care. However, randomized trials evaluating the effects of flexible family visitation models (FFVMs) are scarce. This study aims to compare the effectiveness and safety of an FFVM versus a restrictive family visitation model (RFVM) on delirium prevention among ICU patients, as well as to analyze its potential effects on family members and ICU professionals.

Methods and analysis: A cluster-randomized crossover trial involving adult ICU patients, family members, and ICU professionals will be conducted. Forty medical-surgical Brazilian ICUs with RFVMs (<4.5 h/day) will be randomly assigned to either an RFVM (visits according to local policies) or an FFVM (visitation during 12 consecutive hours per day) group at a 1:1 ratio. After enrollment and follow-up of 25 patients, each ICU will be switched over to the other visitation model, until 25 more patients per site are enrolled and followed. The primary outcome will be the cumulative incidence of delirium among ICU patients, measured twice a day using the Confusion Assessment Method for the ICU. Secondary outcome measures will include daily hazard of delirium, ventilator-free days, any ICU-acquired infections, ICU length of stay, and hospital mortality among the patients; symptoms of anxiety and depression and satisfaction among the family members; and prevalence of burnout symptoms among the ICU professionals. Tertiary outcomes will include need for antipsychotic agents and/or mechanical restraints, coma-free days, unplanned loss of invasive devices, and ICU-acquired pneumonia, urinary tract infection, or bloodstream infection among the patients; self-perception of involvement in patient care among the family members; and satisfaction among the ICU professionals.

Ethics and dissemination: The study protocol has been approved by the research ethics committee of all participant institutions. We aim to disseminate the findings through conferences and peer-reviewed journals.

Trial registration: ClinicalTrials.gov, NCT02932358, Registered 11 October 2016.

Keywords: delirium, family, health personnel, critical care, intensive care unit

Strengths and limitations of this study:

- The present study is the first large-scale trial aimed to evaluate the effects of different ICU visiting policies on relevant outcomes among patients, family members and ICU professionals.
- This study is designed as a cluster-randomized crossover trial, which reduces the risk of contamination and improves covariate balance between the two study arms and statistical efficiency.
- This study uses strategies to enhance the implementation and evaluation of complex interventions such as some degree of adaptability to local circumstances, a learning period to study interventions, and assessment of fidelity and quality of the implementations.
- The infeasibility of blinding patients, family members and ICU professionals to the study interventions is a limitation.
- The results of this study will allow health care professionals, researchers, and policymakers to draw conclusions about the efficacy and safety of a flexible family visitation model for delirium prevention in adult ICUs.

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LIST OF ABBREVIATIONS

APACHE-II	Acute Physiology and Chronic Health Evaluation II
BRICNet	Brazilian Research in Intensive Care Network
CAM-ICU	Confusion Assessment Method for the ICU
CCFNI	Critical Care Family Needs Inventory
FFVM	Flexible Family Visitation Model
HADS	Hospital Anxiety and Depression Scale
ICC	Intraclass Correlation Coefficient
ICU	Intensive Care Unit
MBI	Maslach Burnout Inventory
PRE-DELIRIC	PREdiction of DELIRium in ICU patients
RASS	Richmond Agitation Sedation Scale
RFVM	Restrictive Familiar Visitation Model
SPIRIT	Standard Protocol Items: Recommendations for Interventional Trials

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INTRODUCTION

Adult intensive care unit (ICU) visitation policies vary worldwide; generally, patients admitted to the ICU are only allowed visitors during certain periods of the day.[1-3] Congruent with this scenario, most Brazilian ICUs have a restrictive policy of family visits in which visiting hours typically last from 30 min to 1 h, two to three times a day.[4] These restrictive ICU-visit policies are rooted mainly in a theoretical increased risk of physiological stress, infectious complications, and disorganization of care.[5] However, these theoretical risks have not been consistently confirmed by the scarce literature on this subject,[6-9] and flexible ICU visiting hours have been proposed as a means to improve outcomes through patient- and family-centered care and delirium prevention.[10-12]

Evidence from small observational and before-and-after studies suggests that flexible ICU visitation policies are associated with higher satisfaction among patients and patients' families and with reduction of patient stress.[13, 14] Accordingly, one pilot randomized trial showed reduction in cardiocirculatory complications among ICU patients admitted during periods of unrestricted visiting hours, possibly due to reduction of anxiety and establishment of a more favorable hormonal profile.[6] Moreover, some studies suggest the potential role of presence of family members as a strategy to prevent ICU delirium.[15-17] One small prospective single-center before-and-after study found a reduction of 50% in the cumulative incidence of delirium by changing the visitation policy from a restrictive model (4.5 h/day) to an extended model (12 h/day); the length of delirium and ICU stay was also reduced in this study.[12] In this regard, the presence of family in the critical care setting is suggested as a means to achieve better pain control, reduce the use of sedatives, and participate in the re-orientation and cognitive stimulation of patients. These benefits have been associated with lower incidence of

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delirium in studies evaluating multicomponent non-pharmacological interventions to prevent delirium, and constitute the rationale for the F (Family Engagement and Empowerment) component of the ABCDEF bundle, an evidence-based approach to prevent delirium.[18-21]

Regarding possible risks associated with flexible ICU-visit policies, some studies have shown that ICU professionals sometimes perceive visits as a source of increased workload and disorganization in patient care, instead of considering families as 'one' with the patient and as potential sources of reassurance and comfort.[22-23] In a single center study,[23] 59% of ICU staff members stated that the open visitation policy impaired the organization of patient care, and 72% believed that their work suffered more interruptions due to the extended presence of families in the ICU. Congruent with these data, one before-and-after study with 9 ICUs [24] showed a significant increase in burnout levels among ICU professionals after a partial liberalization of visiting policies. The impact of educational strategies directed to ICU visitors in the context of flexible family visitation policies to prevent disorganization of patient care and burnout among ICU professionals is not known. In relation to the risk of infection, this topic has been evaluated by few underpowered studies.[12, 15, 25] Although one study [15] showed greater environmental microbial contamination during an open policy of ICU visitation, published studies [12, 15, 25] failed to show an association between flexible ICU visiting hours and nosocomial infection. Lastly, the impact of flexible ICU visiting hours on symptoms of anxiety and depression of family members is not well studied: there is plausibility for decreased anxiety and depression with flexible ICU visiting hours as a result of improved access to information and more effective sharing of the decision-making process;[26] conversely, it is also plausible to assume that anxiety and depression will increase as a result of higher exposure of family

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members to complex situations such as terminality and the patient's emotional and physical suffering.[27, 28]

The implementation of a flexible family ICU-visitation policy, although promising due to its low-cost and potential to improve quality of care, is a complex organizational process, given that multiple populations involved in this context may be affected by the intervention in different ways. Additionally, most evidence regarding this intervention is originated from underpowered observational and before-and-after studies. Specifically, no large-scale randomized trial so far has evaluated the potential impact of different ICU visitation models on patient, family, and ICU staff outcomes. We hypothesize that compared to the restrictive family visitation model (RFVM), a flexible family visitation model (FFVM) supported by visitor education will reduce the cumulative incidence of delirium among adult ICU patients, reduce symptoms of anxiety and depression, and increase satisfaction with care among family members without increasing burnout levels among ICU professionals.

OBJECTIVES

Primary objective

The aim of the present study is to assess if an FFVM, compared to an RFVM, can prevent delirium in adult ICU patients.

Secondary objectives

Our secondary objective is to compare the efficacy and safety of both ICU visitation models with regard to three sets of variables: ICU/patient related variables (daily hazard of delirium, ventilator-free days, ICU-acquired infections, ICU length of stay, all-cause hospital mortality, need for antipsychotic use, coma-free days, need for

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mechanical restraints, and unplanned loss of invasive devices), family-related variables (symptoms of anxiety and depression, satisfaction, and self-perception of involvement in patient care), and ICU staff variables (prevalence of symptoms of burnout syndrome and satisfaction).

METHODS

The present study protocol follows the SPIRIT statement recommendations.[29] The items from the World Health Organization trial registration data set are described in Supplementary File 1. This study protocol was registered at clinicaltrials.gov before the randomization of the first cluster (NCT02932358).

Study design

The present study was designed to be a cluster-randomized, crossover trial involving mixed medical-surgical ICUs. In this study, the unit of randomization is the ICU, since the proposed intervention involves components at the organizational level and is intended to be implemented in the whole ICU and not for selected patients. All ICUs will receive both FFVM and RFVM, and the randomization will determine in which order the visitation models will be evaluated in each ICU (Figure 1). The initial intervention (phase 1) will involve ICU randomization to either an FFVM or an RFVM. In phase 2, each ICU will be crossed over to the other visitation model. The study analysis will be performed at the subject level according to the intention-to-treat principle and accounts for the cluster-randomized crossover design.

Participants

Cluster eligibility, recruitment, and exclusion criteria

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Brazilian adult ICUs of public and philanthropic hospitals will be invited to participate in the trial. Mixed medical-surgical ICUs with at least 6 beds and a restrictive policy of family visitation (<4.5 h/day) are considered eligible. ICUs with structural or organizational impediments to flexible family visitation, according to the Brazilian resolution of minimal operational requirements for ICUs,[30] will be excluded.

Patient eligibility, recruitment, and exclusion criteria

Consecutive patients aged ≥18 years admitted to the ICU during phases 1 and 2 will be enrolled in each cluster. Subjects in a coma (Richmond Agitation Sedation Scale [RASS] [31] -4 or -5) lasting >96 h from the moment of first evaluation for recruitment, and those with delirium at baseline (positive Confusion Assessment Method for ICU [CAM-ICU] [32]) will be excluded. The following exclusion criteria will also be applied: cerebral death, aphasia, severe hearing deficit, predicted ICU length of stay <48 h, exclusive palliative treatment at ICU admission, unavailability of a family member to participate in the flexible family visits, unlikelihood to survive >24 h, prisoner status, and lastly, readmission to the ICU after enrolment in the study.

Family member eligibility, recruitment, and exclusion criteria

The sample of family members will include one family member per patient enrolled into the study, with the closest family member being selected. Family members who do not speak Portuguese or have serious impediment in answering the self-applied questionnaires (e.g., illiteracy or severe visual or hearing limitations) will be excluded.

ICU professionals' eligibility, recruitment, and exclusion criteria

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All bedside ICU professionals (physicians, nurses, nursing technicians, and physiotherapists) of each cluster who assist patients during the daytime for at least 20 h per week will be enrolled. ICU professionals who have a planned leave of absence of >15 days during phase 1 will be excluded.

Interventions

The proposed study interventions may be classified as complex because:[33] (a) there is a large number of interacting components within the experimental and control interventions (e.g., changes in ICU processes, education of family members, and engagement and training of the ICU multidisciplinary team); (b) there are several groups targeted by the intervention (ICU patients, family members and ICU professionals); (c) there is a large number and high variability of outcomes (evaluation of different outcome domains in three different target populations); (d) a limited degree of flexibility in the intervention is allowed (educational components may be tailored considering the educational level of the target population, visit hours may be customized according to internal processes of the ICU and expected acceptability of the target population).

We tested the feasibility and acceptability of implementation of the intervention in a single center before-and-after study.[12] Table 1 shows the components to be implemented during FFVM and RFVM. During both FFVM and RFVM, all visitors will be required to perform hand hygiene by washing their hands with antiseptic soap or using alcohol-based hand-rub formulations, and to wear disposable vests and/or personal protective equipment when appropriate (e.g., contact or droplet precautions). All visitors will receive oral and written guidance about the minimum requirements to promote a safe and restful environment to ICU patients. The

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visitors will be asked to leave the room during some procedures such as intubation, central venous or urinary catheterization, bronchoscopy, electrical cardioversion, and cardiopulmonary resuscitation. As an exception, some patients, during both study interventions, will be allowed to receive visits longer than the maximum limit of visiting hours. This decision will be allowed in the following situations: patient age ≥65 years, terminal illness, and conflicts among patients or family and ICU staff.

Table 1. Components of study interventions

	RFVM	FFVM
Social visits	X	X
Friends and family members allowed (number of simultaneous visitors allowed in patient's room tailored to ICU preferences)		
Max 4.5 hours per day (according to ICU policies prior to randomization)		
Family visits		X
Up to 2 family members allowed (number of simultaneous visitors allowed in patient's room tailored to ICU preferences)		
Maximum of 12 hours per day		
Family members must attend a structured information meeting		
Information meeting		X
For family members who want to participate in the family visits		
Guidance about ICU environment, multidisciplinary work at ICU, common ICU treatments, palliative care, infection control practices, delirium prevention and rehabilitation		
Meeting conducted by a trained healthcare professional that works in the ICU (at least 3x/week)		

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	RFVM	FFVM
Both printed and digital material offered by the study coordinator site (tailored for the specific ICU preferences)		
Printed material focused on patient safety during ICU visits	X	X
Brochure with information about what is allowed and what is not allowed in a social visit		
Printed material focused on education about ICU environment, practices and family engagement on patient care		X
Brochure with information about ICU environment, multidisciplinary work at ICU, common ICU treatments, palliative care, infection control practices, delirium prevention, rehabilitation and family engagement on patient care		
Access to a website focused on education about ICU environment, practices and family engagement on patient care		X
Website with information about ICU environment, multidisciplinary work at ICU, common ICU treatments, palliative care, infection control practices, delirium prevention, rehabilitation and family engagement on patient care		

FFVM, flexible family visitation model; RFVM, restrictive family visitation model.

Flexible Family Visitation Model (FFVM)

In the FFVM, two or fewer close family members will be allowed to visit the patient for up to 12 consecutive hours each day. Family members who agree to join the family visits will have to attend a structured meeting at the ICU in which they will receive guidance about the ICU environment, common ICU treatments, rehabilitation and basic infection control practices, multidisciplinary work at the ICU, and information on palliative care and delirium prevention. Additionally, family members will receive an information brochure and be encouraged to access a website

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(www.utivisitas.com.br), both of which are designed to explain, in simple terms, what happens during and after an ICU stay to legitimize emotions and improve cooperation with relatives without increasing the ICU-staff workload. In addition to family visitation, patients in the FFVM will be allowed to receive social visits at specific time intervals (according to the local ICU policies). Social visits will be offered to patient's friends or other family members that did not qualify for family visitation. The number and duration of social visits will be determined by the patient or proxies. Social visitors will not be required to attend the structured meeting.

Restrictive Family Visitation Model (RFVM)

In the RFVM, patients will be allowed visitors according to routine ICU practices, but limited to the maximum of 4.5 h of visitation per day. Visitors will not be required to attend the structured meeting, because this is the standard of care in Brazil. The length of ICU visiting hours will be similar to that of social visits in the FFVM. The number and duration of visits will be determined by the patient or proxies taking into the account the limits of visiting hours dictated by local policies.

Randomization

The randomization unit is the ICU. In hospitals where there is more than one ICU, each ICU will be considered a distinct randomization units as long as the ICU staff are different. If the staff are the same, all ICUs in the hospital will be considered a single unit of randomization. The allocation of the initial intervention (i.e., FFVM or RFVM) will be performed through blocks of different sizes and stratified by number of ICU beds. A randomization list will be generated, and ICUs will be consecutively randomized as per the date of approval by the local Research Ethics Committee. In

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order to guarantee allocation concealment, a statistician will receive an identification code for each unit but will remain blinded to the identity of the ICU. The statistician will then inform the allocation for each unit identification code to the research coordinator. Lastly, the research coordinator will inform the ICUs regarding the group to which they were initially allocated.

Blinding

It is not feasible to blind the researchers, patients, family members or ICU professionals to the study interventions.

Outcomes

Primary outcome

The primary outcome is the cumulative incidence of delirium during the ICU stay. Diagnosis of delirium will be made using the validated Brazilian translation of the CAM-ICU,[34] which will be applied at least once per 12-h shift in patients with RASS ≥-3, by trained ICU professionals. The cumulative incidence of delirium is defined as the presence of delirium (at least one positive CAM-ICU) on at least one 12-h shift during the ICU stay. Before study initiation, all professionals responsible for CAM-ICU assessment will receive training concerning the CAM-ICU. This specific training will be given both during investigator meetings and on-site. Furthermore, inter-rater reliability measurements of the CAM-ICU and RASS will be performed before study initiation to evaluate the quality of assessments, and, if necessary, additional training will be provided. A sensitivity analysis of the primary outcome adjusted for the baseline risk of developing delirium determined by the PREdiction of DELIRium in ICU patients (PRE-DELIRIC) score [35] will be conducted to check the consistency of the

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results. There will be three a *priori* defined subgroup analyses for the primary endpoint: 1) effectiveness of FFVM vs. RFVM in ICUs according to the PRE-DELIRIC score (patients with a predicted risk <25%, 25-50%, 50–75%, and >75%); 2) effectiveness of FFVM vs. RFVM in ICUs according to patient group (medical vs. surgical, and neurocritical vs. non-neurocritical); and (3) effectiveness of FFVM vs. RFVM in ICUs according to Acute Physiology and Chronic Health Evaluation II (APACHE-II) scores (≤15 vs. >15 points). Additional exploratory subgroup analysis will be performed based on the level of patient's exposure to sedation, ICU professional's workload and proportion of private ICU beds.

Secondary outcomes

Secondary outcome measures include daily hazard of delirium, ventilator-free days, any ICU-acquired infections (pneumonia or urinary tract infection or bloodstream infection according to Centers for Disease Control and Prevention guidelines [36-38]), ICU length of stay, and all-cause hospital mortality among patients; symptoms of anxiety and depression measured by the Hospital Anxiety and Depression Scale (HADS) [39] and satisfaction measured by the Critical Care Family Needs Inventory (CCFNI) [40] among family members; and prevalence of symptoms of burnout syndrome measured by the Maslach Burnout Inventory (MBI) [41] among ICU professionals. The daily hazard of delirium will be evaluated using a joint modelling approach [42] which is recommended to account for days at risk for delirium (i.e., ICU days in a non-comatose state).

All cases of ICU-acquired infections will be adjudicated by an infectious disease physician blinded to the study interventions. Family members and ICU professionals will be evaluated through self-administered questionnaires.

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Tertiary outcomes

Tertiary outcomes will include need for antipsychotic agents and/or mechanical restraints, coma-free days, unplanned loss of invasive devices, and ICU-acquired pneumonia, urinary tract infection, or bloodstream infection among ICU patients; self-perception of involvement in patient care (i.e., re-orientation activities, pain control, mobilization, feeding, comfort, emotional support, and communication [helping patients to interpret ICU-staff orientations, and ICU professionals to understand patient needs]) among family members; and satisfaction among ICU workers.

Length of ICU intervention, participant recruitment, and timeline, data collection, management, and monitoring

The length of study phases will be determined by the patient recruitment rate. During phase 1, 25 patients per ICU will be enrolled. After enrollment of the 25th patient, a 30-day period without subject recruitment (i.e., washout period) will occur to allow appropriate conclusion of the follow-up of all recruited patients for the study outcomes and to avoid contamination of the two study arms. After this period, each ICU will be crossed over to the other visitation model (phase 2), with enrollment of an additional 25 ICU patients per ICU.

The study flow diagram is showed in Figure 2 and the schedule of enrollment, interventions and assessments is showed in Supplementary File 2. Patients and family members will be recruited during phases 1 and 2. ICU professionals will be evaluated and followed up only during the phase 1 in order to avoid the carry-over effect. Patients will be followed up from study enrollment to hospital discharge or death, or a maximum of 30 days. Family members will be evaluated at two time points: within the first 48 h

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of patient inclusion into the study (for baseline data) and within 7 days from patient discharge from ICU or death, or a maximum of 30 days (for outcomes assessment). ICU professionals will be evaluated at two time points: 2 weeks before initiation of the first randomized ICU intervention (for baseline data) and during phase 1 (for outcome assessment).

Trained research personnel at the local sites will prospectively collect data on printed case report forms that will be entered into an electronic data capture system (REDCap, Vanderbilt University, Tennessee, USA).[43] In order to allow intention-to-treat analyses, data will be collected and analyzed independent of adherence to study interventions. We will deploy the following procedures to enhance the implementation of study interventions and ensure data quality:

1. All local principal investigators and sub investigators will attend an on-site training session before the beginning of the study to standardize procedures including data collection.
2. All ICUs will have a learning period within the first 15 days of phases 1 and 2. During this period, ICUs will receive the intervention (FFVM or RFVM) but will not recruit subjects. Local investigators will use this period to adapt the ICU staff to the organizational aspects of study intervention, including rules about visiting hours (for both FFVM and RFVM periods), guidance to visitors about the minimum requirements to promote a safe and restful environment to ICU patients (for both FFVM and RFVM periods), role of ICU professionals during family visiting hours (for FFVM period), and conduction of family-members-directed structured meetings (for FFVM period). Furthermore, local investigators will use this period to test the study measurements (CAM-ICU, HADS, CCFNI, MBI) and address concerns

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regarding case-report filling.

3. The investigators will be able to contact the Coordinating Center to solve any potential issues or problems.
4. Data cleaning will be applied continuously to identify inconsistencies and missing data. The centers will be notified of any inconsistencies and missing data and prompted to solve them.
5. The Coordinating Center will review detailed reports on screening, inclusion, follow-up, and data consistency and completeness on a weekly basis. The Coordinating Center will take immediate action to solve any problems.
6. Centers will be monitored throughout the study. On-site monitoring visits will occur during phases 1 and 2. A trained professional appointed by the Coordinating Center will perform the monitoring visit. During the monitoring visits, all information will be considered strictly confidential.

To assess the fidelity and quality of the proposed interventions, we will perform on-site monitoring visits, with a standardized checklist, in order to evaluate if the processes are consistent with the intended intervention or if there are important deviation from the proposed protocol; perception of effectiveness and barriers for implementation will be assessed qualitatively, through semi-structured interviews with healthcare professionals involved in the study.[44] In addition, we will collect data related to the length of visits for included patients, study website access, and family members characteristics. A data monitoring committee is not required as the risk of study interventions causing significant harms is low.

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Sample size and sampling

A minimum of 33 ICUs with recruitment rate of 50 patients per ICU (25 patients per study phase) will be needed (total of 1,650 patients) to detect an absolute difference >6.0% in the cumulative incidence of delirium between the two study arms (considering an outcome incidence rate of 20.5% in the RFVM), with 80% power, and two-tailed 0.05 alfa. Two levels of intraclass correlation coefficient (ICC) were considered to calculate the sample size: 0.05 for subjects in the same cluster/time period and 0.01 for subjects in the same cluster/different time periods. Estimates of sample size for the primary outcome were made on the basis of the cumulative incidence of delirium found in a single center before-and-after study that evaluated the effect of different policies of family visitation on the incidence of delirium.[12] In order to compensate for potential ICU and patient losses, the present study plans to recruit 40 ICUs.

Statistical analysis

A detailed statistical analysis plan will be prepared before data analysis and is intended to be published or made available online. All analyses will be conducted with the intention-to-treat principle. The comparison of cumulative incidence of delirium will be performed using models for correlated data considering the ICU as a cluster and presented as risk ratios and 95% confidence intervals. The same models will be used for analysis of secondary and tertiary outcomes, i.e., considering the ICU as a cluster and each outcome with its adequate probability distribution. A statistical significance level of 0.05 will be adopted for all statistical comparisons. The R-Development Core Team will be used for analysis.

DISCUSSION AND TRIAL STATUS

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Flexible ICU visiting policy of is a complex intervention, with multiple components, targeting different populations with specific outcomes. Figure 3 describes the logic model for the FFVM. Although several outcomes are expected to have a positive impact, we chose incidence of delirium as primary outcome because it combines a strong potential for causal and direct association and an important clinical impact. Delirium is a highly prevalent ICU complication and is associated with increased mortality, longer ICU and hospital stay, higher cost of care, and long-term cognitive impairment.[45-47] Therefore, identifying interventions that may reduce the risk and burden of delirium in ICU patients is of paramount importance to improve health-care quality. Other important outcomes, such as ICU-acquired infections and length of stay, levels of burnout among ICU professionals, and symptoms of anxiety and depression and satisfaction among family members may have both a direct and indirect relation with the proposed intervention and, therefore, may represent important markers of effectiveness and safety of the proposed intervention. An FFVM rooted in education of family members may reduce the theoretical risk of increase in ICU staff workload, disorganization of care, and ICU-acquired infections. The higher access to information may have a positive effect on family members' satisfaction and interactions with the patients and ICU professionals. Moreover, an FFVM may result in shorter ICU stay, mediated, for instance, by a lower incidence of delirium; additionally, a better understanding of the condition by the family may avoid delays in ICU discharge.

To the best of our knowledge, this will be the first large-scale, multicenter randomized trial evaluating the effects of different policies of ICU visitation on patients, family members and ICU professionals. Results of this study will allow health care professionals, researchers, and police makers to draw conclusions about the efficacy and safety of a flexible family visitation model in adult ICUs.

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Our study has some limitations. First, high variability across institutions is expected; although the chosen ICCs may be considered conservative, there are no estimates in the literature for the proposed intervention, which may result in lack of power if the actual ICC is larger than the estimate. Also, no masking of outcome assessors may result in measurement bias for delirium specially with the use of an instrument with some degree of subjectivity [48]; although blinding is not feasible for the proposed intervention, in order to minimize risk of bias we chose validated methods for delirium evaluation and will make efforts in order to standardize data collection through continuing education of outcome evaluators. As the number of patients is small for each cluster, the estimate time for data collection for each study phase is from two to three months; this length of time may not be enough to properly assess burnout in healthcare professionals. Finally, our trial is not designed to evaluate long-term outcomes, such as PTSD in patients and family members, as well as microbiological changes in ICU flora due to a higher circulation of individuals from the community. These issues should be assessed in future studies.

The study design and protocol were finalized in March 2016, and the protocol was approved by the Research Ethics Committee in April 2016. All site investigators were required to participate in at least one of two investigator meetings (November 2016 and April 2017). Currently, this study is recruiting subjects in 34 ICUs representative of the Brazilian geopolitical territory (Figure 4). Another 6 ICUs are in the process of preparation for study initiation. We expect that this study will be completed in June 2018.

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ETHICS AND DISSEMINATION

Ethics approval and consent to participate

This study will be conducted according to the resolution no. 466/12 of the Brazilian National Health Council (http://bvsms.saude.gov.br/bvs/saudelegis/cns/2013/res0466_12_12_2012.html). The present study protocol version (version 3, from 22 February 2017) has been approved by the Research Ethics Committee of the coordinating site (approval number: CAAE 57717516.3.1001.5330) and the research ethics committees of all participant institutions (Supplementary File 3). The need for patients' written informed consent was waived in 37 of 40 participating ICUs, because the standard of care encompasses both study interventions. In 3 of 40 ICUs informed consent will be required for patients or proxies. Informed consent will be required for family members and ICU professionals in all ICUs. Site investigators will be responsible for obtaining informed consent from study participants. Subject confidentiality will be assured through data anonymization and controlled access to case report forms, electronic data capture system, and datasets. Any breaches of confidentiality, study protocol, or adverse events attributable to this study will be reported to the above research ethics committees.

Dissemination

We hope to make the study findings widely available and plan to disseminate our results in international conferences and peer-reviewed journals. Authors and collaborators will be involved in reviewing drafts of the manuscripts, press releases and any other publication format arising from this study.

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FOOTNOTES

Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

RGR, CT, and DBS developed the main study intervention (FFVM). RGR, CT and MF developed the original concept of this study. RGR, MF, NB, ABC, FB, LCPA, FRM, JIS, JASP, RBM, and CT contributed to study design. RGR, LGL and CT wrote the first draft of the first draft of the paper, and MF, NB, ABC, FB, LCPA, FRM, JIS, JASP, RBM, CCR, RK, RMM, MMSS, DS, NEG, CE, TR, TH, AA, JMMT, MGB, DCB, ILF, VN, HMV, LCC, PADD, RT, SLSB, and AG revised the first draft. The final manuscript was reviewed by all the authors. All authors read and approved the final manuscript.

Composition and role of the steering committee

The steering committee of ICU Visits study consists of RGR, MF, CCR, ABC, FB, LCPA, FRM, JIS, JASP, RBM, NB, and CT. The role of the steering committee in the present trial is to provide oversight of the conduct of the study. Specific responsibilities of the steering committee include overall supervision of the trial progress and reduction of protocol deviations to a minimum.

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Role of the coordinating center

The coordination center of this study (Hospital Moinhos de Vento) is responsible for research materials development, data management, monitoring and communication among all sites, and supervision of the conduct of the trial.

Funding

The present study was funded by the Brazilian Ministry of Health through the Program of Institutional Development of the Brazilian Unified Health System (PROADI-SUS).

Role of the funder/sponsor

The funding agency approved the study design and participated in the selection of participant ICUs. The funding agency will have no role in study conduction; collection, management, analysis, and interpretation of the data; and preparation of the manuscript. The funding agency will revise the final version of the manuscript before submission for publication.

Competing interests

The authors declare that they have no competing interests.

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REFERENCES

1. Liu V, Read JL, Scruth E, et al. Visitation policies and practices in US ICUs. *Crit Care* 2013;17:R71. doi: 10.1186/cc12677

2. Garrouste-Orgeas M, Vinatier I, Tabah A, et al. Reappraisal of visiting policies and procedures of patient's family information in 188 French ICUs: a report of the Outcomerea Research Group. *Ann Intensive Care* 2016;6:82. doi: 10.1186/s13613-016-0185-x

3. Spreen AE, Schuurmans MJ. Visiting policies in the adult intensive care units: a complete survey of Dutch ICUs. *Intensive Crit Care Nurs* 2011;27:27-30. doi: 10.1016/j.iccn.2010.10.002

4. Ramos FJ, Fumis RR, de Azevedo LC, et al. Intensive care unit visitation policies in Brazil: a multicenter survey. *Rev Bras Ter Intensiva* 2014;26:339-46. doi: 10.5935/0103-507X.20140052

5. Berwick DM, Kotagal M. Restricted visiting hours in ICUs: time to change. *JAMA* 2004;292:736-7. doi: 10.1001/jama.292.6.736

6. Fumagalli S, Boncinelli L, Lo Nostro A, et al. Reduced cardiocirculatory complications with unrestrictive visiting policy in an intensive care unit: results from a pilot, randomized trial. *Circulation* 2006;113:946-52. doi: 10.1161/CIRCULATIONAHA.105.572537

7. Malacarne P, Corini M, Petri D. Health care-associated infections and visiting policy in an intensive care unit. *Am J Infect Control* 2011;39:898-900. doi: 10.1016/j.ajic.2011.02.018

8. Giannini A, Miccinesi G, Prandi E, et al. Partial liberalization of visiting policies and ICU staff: a before-and-after study. *Intensive Care Med* 2013;39:2180-7. doi: 10.1007/s00134-013-3087-5

For peer review only

9. da Silva Ramos FJ, Fumis RR, Azevedo LC, et al. Perceptions of an open visitation policy by intensive care unit workers. *Ann Intensive Care* 2013;3:34. doi: 10.1186/2110-5820-3-34

10. Levy MM, De Backer D. Re-visiting visiting hours. *Intensive Care Med* 2013;39:2223-5. doi: 10.1007/s00134-013-3119-1

11. Giannini A, Garrouste-Orgeas M, Latour JM. What's new in ICU visiting policies: can we continue to keep the doors closed? *Intensive Care Med* 2014;40:730-3. doi: 10.1007/s00134-014-3267-y

12. Rosa RG, Tonietto TF, da Silva DB, et al. Effectiveness and safety of an extended ICU visitation model for delirium prevention: A Before and After Study. *Crit Care Med* 2017;45:1660-7.

13. Chapman DK, Collingridge DS, Mitchell LA, et al. Satisfaction with elimination of all visitation restrictions in a mixed-profile intensive care unit. *Am J Crit Care* 2016;25:46-50. doi: 10.4037/ajcc2016789

14. Gonzalez CE, Carroll DL, Elliott JS, et al. Visiting preferences of patients in the intensive care unit and in a complex care medical unit. *Am J Crit Care* 2004;13:194-8.

15. Eghbali-Babadi M, Shokrollahi N, Mehrabi T. Effect of family-patient communication on the incidence of delirium in hospitalized patients in cardiovascular surgery ICU. *Iran J Nurs Midwifery Res* 2017;22:327-31. doi: 10.4103/1735-9066.212985

16. Van Rompaey B, Elseviers MM, Schuurmans MJ, et al. Risk factors for delirium in intensive care patients: a prospective cohort study. *Crit Care* 2009;13:R77. doi: 10.1186/cc7892

For peer review only

17. Martinez FT, Tobar C, Beddings CI, et al. Preventing delirium in an acute hospital using a non-pharmacological intervention. *Age Ageing* 2012;41:629-34. doi: 10.1093/ageing/afs060

18. Balas MC, Vasilevskis EE, Olsen KM, et al. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Crit Care Med* 2014;42:1024-36. doi: 10.1097/CCM.0000000000000129

19. Trogrlic Z, van der Jagt M, Bakker J, et al. A systematic review of implementation strategies for assessment, prevention, and management of ICU delirium and their effect on clinical outcomes. *Crit Care* 2015;19:157. doi: 10.1186/s13054-015-0886-9

20. Brummel NE, Girard TD. Preventing delirium in the intensive care unit. *Crit Care Clin* 2013;29:51-65. doi: 10.1016/j.ccc.2012.10.007

21. Siddiqi N, Harrison JK, Clegg A, et al. Interventions for preventing delirium in hospitalised non-ICU patients. *Cochrane Database Syst Rev* 2016;3:CD005563. doi: 10.1002/14651858.CD005563.pub3

22. Davidson JE, Aslakson RA, Long AC. Guidelines for family-centered care in the neonatal, pediatric, and adult ICU. *Crit Care Med* 2017; 45(1):103-128. doi: 10.1097/CCM.0000000000002169

23. Ramos FJ, Fumis RR, Azevedo LC, et al. Perceptions of an open visitation policy by intensive care unit workers. *Ann Intensive Care* 2013;3:34. doi: 10.1186/2110-5820-3-34

24. Giannini A, Miccinesi G, Prandi E, et al. Partial liberalization of visiting policies and ICU staff: a before-and-after study. *Intensive Care Med* 2013;39:2180-7. doi: 10.1007/s00134-013-3087-5

For peer review only

25. Malacarne P, Corini M, Petri D. Health care-associated infections and visiting policy in an intensive care unit. *Am J Infect Control* 2011;39:898-900. doi: 10.1016/j.ajic.2011.02.018

26. Lautrette A, Darmon M, Megarbane B, et al. A communication strategy and brochure for relatives of patients dying in the ICU. *N Engl J Med* 2007;356:469-78. doi: 10.1056/NEJMoa063446

27. Pochard F, Azoulay E, Chevret S, et al. Symptoms of anxiety and depression in family members of intensive care unit patients: ethical hypothesis regarding decision-making capacity. *Crit Care Med* 2001;29:1893-7.

28. Rosendahl J, Brunkhorst FM, Jaenichen D, et al. Physical and mental health in patients and spouses after intensive care of severe sepsis: a dyadic perspective on long-term sequelae testing the Actor-Partner Interdependence Model. *Crit Care Med* 2013;41:69-75. doi: 10.1097/CCM.0b013e31826766b0

29. Chan AW1, Tetzlaff JM, Altman DG, et al. SPIRIT 2013 statement: defining standard protocol items for clinical trials. *Ann Intern Med* 2013;158:200-7. doi: 10.7326/0003-4819-158-3-201302050-00583

30. Ministério da Saúde. Agência Nacional de Vigilância Sanitária (Brazil). Resolução nº 7, de 24 fevereiro de 2010. Dispõe sobre os requisitos mínimos para funcionamento de Unidades de Terapia Intensiva e dá outras providências. Brasília (DF): Ministério da Saúde; 2010. http://bvsms.saude.gov.br/bvs/saudelegis/anvisa/2010/res0007_24_02_2010.html. (accessed 27 Nov 2017).

31. Sessler CN, Gosnell MS, Grap MJ, et al. The Richmond Agitation-Sedation Scale: validity and reliability in adult intensive care unit patients. *Am J Respir Crit Care Med* 2002;166:1338-44. doi: 10.1164/rccm.2107138

For peer review only

32. Ely EW, Margolin R, Francis J, et al. Evaluation of delirium in critically ill patients: validation of the Confusion Assessment Method for the Intensive Care Unit (CAM-ICU). *Crit Care Med*. 2001;29:1370-9.

33. Craig P, Dieppe P, Macintyre S, et al. Developing and evaluating complex interventions: the new Medical Research Council guidance. *BMJ* 2008;337:a1655. doi: 10.1136/bmj.a1655

34. Gusmao-Flores D, Salluh JI, dal-Pizzol F, et al. Validity and reliability of the Brazilian-Portuguese version of three tools to diagnose delirium: CAM-ICU, CAM-ICU Flowsheet and ICDSC. *Crit Care* 2011;15:50. doi: 10.1186/cc10198

35. van den Boogaard M, Pickkers P, Slooter AJ, et al. Development and validation of PRE-DELIRIC (PREdiction of DELIRium in ICu patients) delirium prediction model for intensive care patients: observational multicentre study. *BMJ* 2012;344:e420. doi: 10.1136/bmj.e420

36. Centers for Disease Control and Prevention. Bloodstream Infection Event (Central Line-Associated Bloodstream Infection and non-central line-associated Bloodstream Infection). 2017. https://www.cdc.gov/nhsn/pdfs/pscmanual/4psc_clabscurrent.pdf. (accessed 27 Nov 2017).

37. Centers for Disease Control and Prevention. Pneumonia (Ventilator-associated [VAP] and non-ventilator-associated Pneumonia [PNEU]) Event. 2017. https://www.cdc.gov/nhsn/pdfs/pscmanual/6pscvapcurrent.pdf. (accessed 27 Nov 2017).

38. Centers for Disease Control and Prevention. Urinary Tract Infection (Catheter-Associated Urinary Tract Infection [CAUTI] and Non-Catheter-Associated Urinary Tract Infection [UTI]) and Other Urinary System Infection [USI]) Events. 2017.

For peer review only

https://www.cdc.gov/nhsn/pdfs/pscManual/7pscCauticurrent.pdf. (accessed 27 Nov 2017)

39. Botega NJ, Bio MR, Zomignani MA, et al. Mood disorders among medical in-patients: a validation study of the hospital anxiety and depression scale (HAD). *Rev Saude Publica* 1995;29:355-63.

40. Fumis RR, Nishimoto IN, Deheinzelin D. Measuring satisfaction in family members of critically ill cancer patients in Brazil. *Intensive Care Med* 2006;32:124-8. doi: 10.1007/s00134-005-2857-0

41. Campos JA, Maroco J. [Maslach Burnout Inventory - Student Survey: Portugal-Brazil cross-cultural adaptation]. *Rev Saude Publica* 2012;46:816-24.

42. Colantuoni E, Dinglas VD, Ely EW, et al. Statistical methods for evaluating delirium in the ICU. *Lancet Respir Med* 2016;4(7):534-6. doi: 10.1016/S2213-2600(16)30138-2

43.Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)--a metadata-driven methodology and workflow process for providing translational research informatics support. *J Biomed Inform* 2009;42:377-81. doi: 10.1016/j.jbi.2008.08.010

44. Moore GF, Audrey S, Barker M, et al. Process evaluation of complex interventions: Medical Research Council guidance. *BMJ* 2015;350:h1258. doi: 10.1136/bmj.h1258

45. Reade MC, Finfer S. Sedation and delirium in the intensive care unit. *N Engl J Med* 2014;370:444-54. doi: 10.1056/NEJMra1208705

46. Salluh JI, Soares M, Teles JM, et al. Delirium epidemiology in critical care (DECCA): an international study. *Crit Care* 2010;14:R210. doi: 10.1186/cc9333

For peer review only

761 47. Salluh JI, Wang H, Schneider EB, et al. Outcome of delirium in critically ill
762 patients: systematic review and meta-analysis. *BMJ* 2015;350:h2538. doi:
763 10.1136/bmj.h2538
764 48. Van Eijk MM, Van den Boogaard M, Van Marum RJ, et al. Routine use of the
765 confusion assessment method for the intensive care unit: a multicenter study. *Am J*
766 *Respir Crit Care Med* 2011;184(3):340-4. doi: 10.1164/rccm.201101-0065OC

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FIGURE LEGENDS

Figure 1. Study design.

FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model.

During the study, the ICU intervention (FFVM or RFVM) will be applied to all admitted patients apart of meeting inclusion criteria for the study. The length of study phases in each ICU will be determined by the patient recruitment rate (25 patients in phase 1 and 25 patients in phase 2). Patients and family members will be recruited during phases 1 and 2. ICU professionals will be evaluated and followed up only during the phase 1. Following the recruitment of the 25th patient, during phase 1, a 30-day period without subject recruitment will occur to allow appropriate conclusion of the follow-up of all recruited patients for the study outcomes and to avoid contamination of the two study arms.

Figure 2. Study flow diagram.

FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model.

Figure 3. Logic model for flexible ICU-visiting hours.

FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model.

Figure 4. Geographical distribution of participating ICUs.

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SUPPLEMENTARY MATERIAL

Supplementary File 1. Items from the World Health Organization trial registration data set.

Supplementary File 2. Schedule of enrollment, interventions, and assessments.

Supplementary File 3. Research ethics committees of the ICU visits study.

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* Collaborators cited by study site (Brazilian estate).

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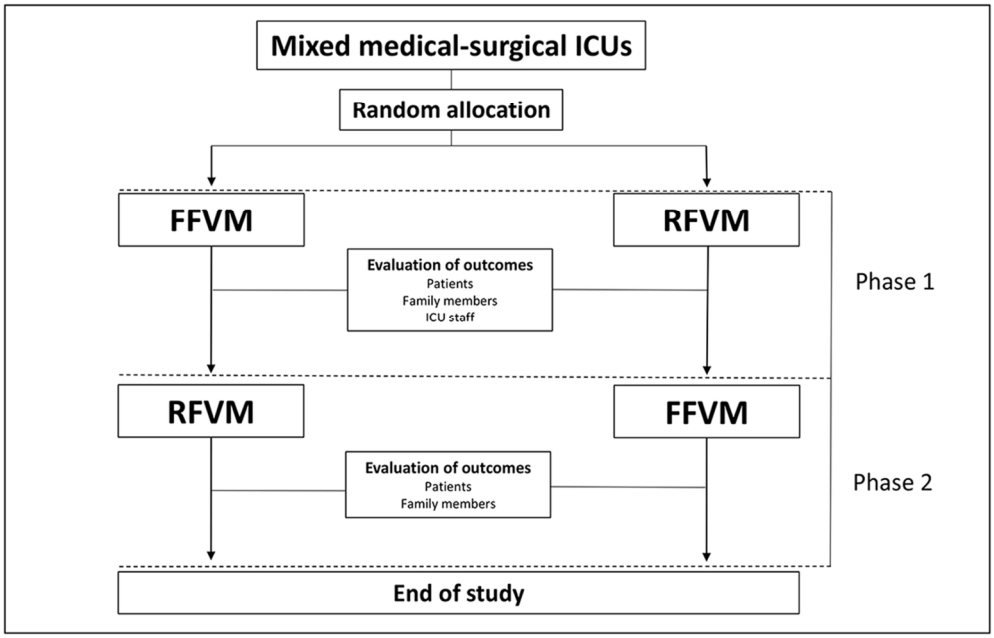

Figure 1. Study design. FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model. During the study, the ICU intervention (FFVM or RFVM) will be applied to all admitted patients apart of meeting inclusion criteria for the study. The length of study phases in each ICU will be determined by the patient recruitment rate (25 patients in phase 1 and 25 patients in phase 2). Patients and family members will be recruited during phases 1 and 2. ICU professionals will be evaluated and followed up only during the phase 1. Following the recruitment of the 25th patient, during phase 1, a 30-day period without subject recruitment will occur to allow appropriate conclusion of the follow-up of all recruited patients for the study outcomes and to avoid contamination of the two study arms.

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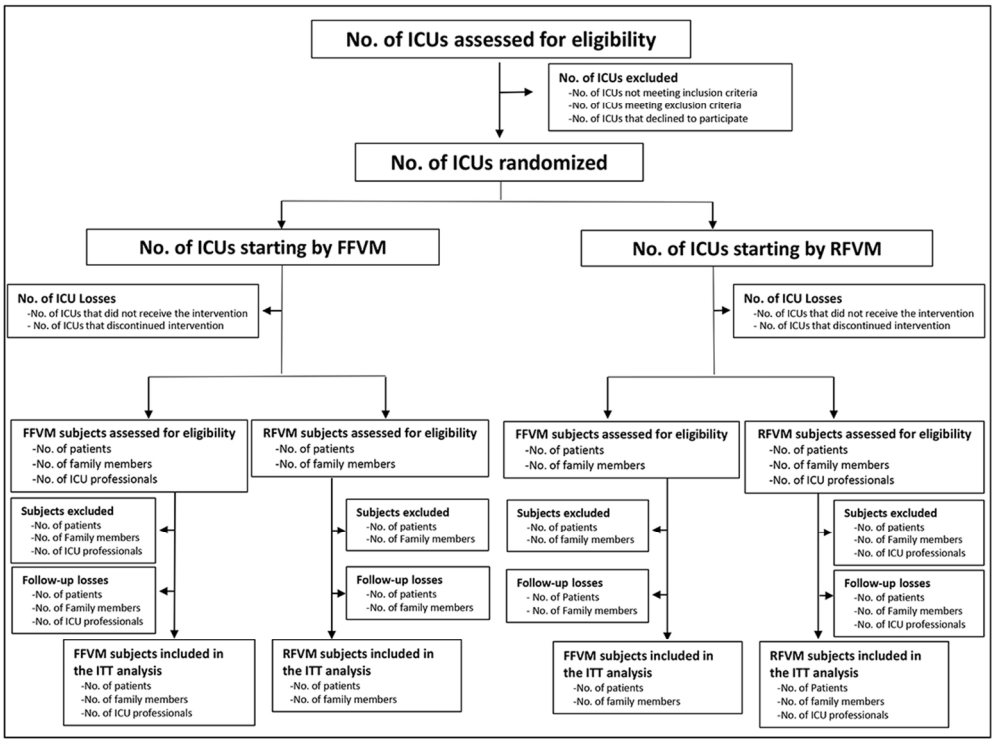

Figure 2. Study flow diagram. FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model.

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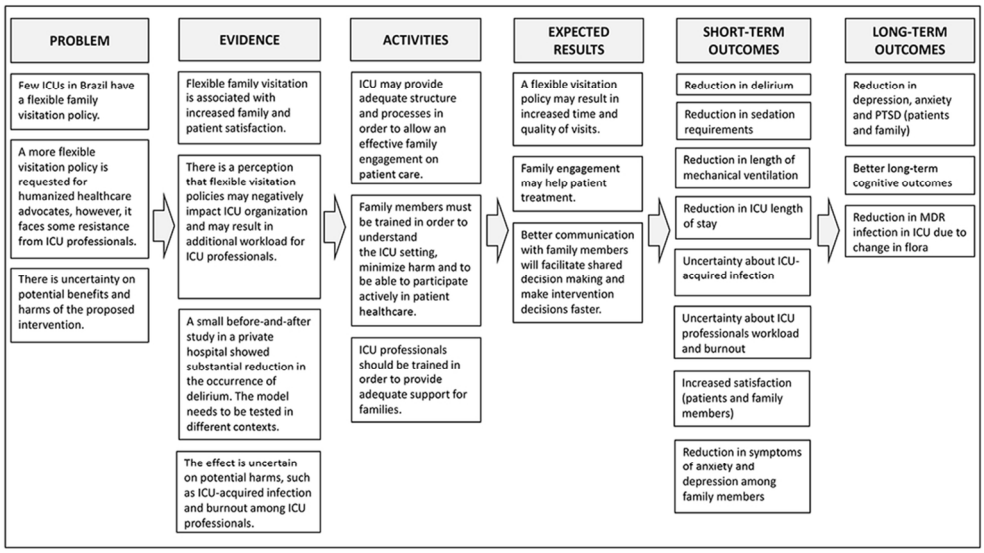

Figure 3. Logic model for flexible ICU-visiting hours. FFVM, flexible family visitation model; ICUs, intensive care units; RFVM, restrictive family visitation model.

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Figure 4. Geographical distribution of participating ICUs.

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Supplementary File 1. Items from the World Health Organization Trial Registration Data Set.

DATA CATEGORY	INFORMATION
Primary registry and trial identifying number	ClinicalTrials.gov NCT02932358
Date of registration in primary registry	11 October 2016
Secondary identifying numbers	CAAE 57717516.3.1001.5330
Source of monetary or material support	The present study was funded by the Brazilian Ministry of Health through the Program of Institutional Development of the Brazilian Unified Health System (PROADI-SUS).
Primary sponsor	Brazilian Ministry of Health
Secondary sponsor	Brazilian Ministry of Health
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Public title	ICU VISITS STUDY
Scientific title	Effectiveness and safety of a flexible family visitation model in adult intensive care units: a cluster-randomized, crossover trial
Countries of recruitment	Brazil
Health conditions or problems studied	Delirium, ICU-acquired infections, anxiety, depression, burnout syndrome.

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Interventions	1) Active comparator: Flexible family visitation model – ICU visitation during 12 consecutive hours per day. 2) Control comparator: Restrictive family visitation model – ICU visitation according to local policies.
Key inclusion and exclusion criteria	1) ICUs - Inclusion criteria: Mixed medical-surgical ICUs with at least 6 beds and a restrictive policy of family visitation (<4.5 h/day). - Exclusion criteria: ICUs with structural or organizational impediments to flexible family visitation. 2) Patients - Inclusion criteria: patients aged ≥18 years admitted to the ICU. - Exclusion criteria: coma lasting > 96hs, cerebral death, aphasia, severe hearing deficit, predicted ICU length of stay <48 h, exclusive palliative treatment at ICU admission, unavailability of a family member to participate in the flexible family visits, unlikelihood to survive >24 h, prisoner status, readmission to the ICU after enrolment in the study. 3) Family members - Inclusion criteria: closest family member of a ICU patient recruited in the study. - Exclusion criteria: family members who do not speak Portuguese or have serious impediment in answering the self-applied questionnaires

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	4) ICU professionals - Inclusion criteria: ICU bedside professionals (physicians, nurses, nursing technicians, and physiotherapists) who assist patients during the daytime for at least 20 h per week. - Exclusion criteria: professionals who have a planned leave of absence of >15 days during the study.
Study type	Interventional Allocation: randomized Intervention model: crossover assignment Masking: open label Primary purpose: prevention
Date of first enrollment	28 April 2017
Target sample size	1650 patients
Recruitment status	Recruiting
Primary outcome	Cumulative incidence of delirium
Key secondary outcomes	Daily hazard of delirium, ventilator-free days, any ICU-acquired infections, ICU length of stay, and all-cause hospital mortality among the patients; symptoms of anxiety and depression and satisfaction among the family members; and prevalence of symptoms of burnout among the ICU professionals.

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Supplementary File 2. Schedule of enrollment, interventions, and assessments.

	Study timeline						
	t1	t2	t3			t4	
	Enrollment of clusters	**Random allocation of clusters**	**Interventions at the cluster level**				
			Phase 1			**Phase 2**	
			Learning curve of phase 1 (15 days)	Recruitment (until the enrollment of the 25th patient)	Period without subject recruitment (30 days)	Learning curve of phase 2 (15 days)	Recruitment (until the enrollment and follow-up of the 50th patient)
ENROLMENT							
Patients				X[1]			X[1]
Family members				X[2]			X[2]
ICU professionals			X				
INTERVENTIONS (cluster level)							
ICUs starting by FFVM							
-FFVM			X	X	X		
-RFVM						X	X
ICUs starting by RFVM							
-FFVM						X	X
-RFVM			X	X	X		
DATA COLLECTION (subjects level)							
Baseline variables							
-Patients				X[1]			X[1]
-Family members				X[2]			X[2]
-ICU professionals			X				
Outcomes							
-Patients				X[3]	X[3]		X[3]
-Family members				X[4]	X[4]		X[4]
-ICU professionals					X		

FFVM, flexible family visitation model; ICU, intensive care unit; RFVM, restrictive family visitation model.

[1] Within the first 48 hours of ICU admission.

[2] Within the first 48hs of patient enrollment.

[3] All patient outcomes will be assessed during the ICU stay, with exception to the hospital mortality, which will be verified at the end of hospitalization.

[4] Within the first 7 days of patient discharge from the ICU.

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Supplementary File 3. Research ethics committees of the ICU visits study.

HOSPITAL (Brazilian estate)	RESEARCH ETHICS COMMITTEE	APPROVAL NUMBER
Hospital de Urgência e Emergência de Rio Branco (AC)	Hospital das Clínicas do Acre - HCA/FUNDHACRE	CAAE 57717516.3.2049.5009
Hospital Geral do Estado Prof. Osvaldo Brandão Vilela (AL)	Hospital Moinhos de Vento - HMV	CAAE 57717516.3.2055.5330
Fundação Hospital Adriano Jorge (AM)	Fundação Hospital Adriano Jorge - FHAJ	CAAE 57717516.3.2021.0007
Hospital Geral Cléríston Andrade (BA)	Secretaria da Saúde do Estado da Bahia - SESAB	CAAE 57717516.3.2028.0052
Incardio - Santa Casa de Misericórdia de Feira de Santana (BA)	Hospital Santa Izabel - Santa Casa de Misericórdia da Bahia	CAAE 57717516.3.2038.5520
Hospital Estadual de Urgência e Emergência do Espírito Santo (ES)	Centro Integrado de Atenção à Saúde - CIAS/UNIMED VITÓRIA	CAAE 57717516.3.2039.5061
Hospital de Urgências de Goiânia (GO)	Hospital de Urgência de Goiânia - HUGO	CAAE 57717516.3.2017.0033
Hospital das Clínicas da Universidade Federal de Minas Gerais (MG)	Universidade Federal de Minas Gerais - UFMG	CAAE 57717516.3.2020.5149
Santa Casa de Misericórdia de São João Del Rei (MG)	Santa Casa de Misericórdia de Juiz de Fora/MG	CAAE 57717516.3.2025.5139

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Hospital Metropolitano de Urgência e Emergência de Ananindeua (PA)	Hospital Moinhos de Vento - HMV	CAAE 57717516.3.2050.5330
Hospital Regional do Baixo Amazonas (PA)	Universidade do Estado do Pará - UEPA - CAMPUS XII - Tapajós	CAAE 57717516.3.2041.5168
Hospital Alberto Urquiza Wanderley (PB)	Hospital Moinhos de Vento - HMV	CAAE 57717516.3.2057.5330
Hospital Universitário Alcides Carneiro (PB)	Hospital Universitário Alcides Carneiro da Universidade Federal de Campina Grande - HUAC /UFCG	CAAE 57717516.3.2026.5182
Hospital Universitário Lauro Wanderley (PB)	Hospital Universitário Lauro Wanderley da Universidade Federal da Paraíba - UFPB	CAAE 57717516.3.2053.5183
Hospital Agamenon Magalhães (PE)	Hospital Agamenon Magalhães - HAM	CAAE 57717516.3.2046.5197
Hospital Universitário da Universidade Federal do Vale do São Francisco (PE)	Fundação Universidade Federal do Vale do São Francisco	CAAE 57717516.3.2034.5196
Hospital Universitário da Universidade Federal do Piauí (PI)	Hospital Universitário da Universidade Federal do Piauí - UFPI	CAAE 57717516.3.2045.8050
Hospital do Câncer de Cascavel (PR)	Associação Paranaense de Cultura - PUCPR	CAAE 57717516.3.2005.0020

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Hospital Universitário do Oeste do Paraná (PR)	Centro de Ciências Biológicas e da Saúde da Universidade Estadual do Oeste do Paraná - UNIOESTE	CAAE 57717516.3.2014.0107
Hospital Geral de Nova Iguaçu (RJ)	Hospital Geral de Nova Iguaçu - HGNI / RJ	CAAE 57717516.3.2009.5254
Hospital Deoclécio Marques de Lucena (RN)	Hospital Universitário Onofre Lopes da Universidade Federal do Rio Grande do Norte - HUOL/UFRN	CAAE 57717516.3.2042.5292
Fundação Saúde Pública São Camilo de Esteio (RS)	Hospital Moinhos de Vento - HMV	CAAE 57717516.3.2051.5330
Hospital Ana Nery (RS)	Hospital Moinhos de Vento - HMV	CAAE 57717516.3.2013.5330
Hospital Conceição (RS)	Hospital Nossa Senhora da Conceição - Grupo Hospitalar Conceição	CAAE 57717516.3.2029.5530
Hospital da Cidade de Passo Fundo (RS)	Universidade de Passo Fundo/ Pró-Reitoria de Pesquisa e Pós-Graduação - VRPPG/ UPF	CAAE 57717516.3.2027.5342
Hospital de Clínicas de Porto Alegre (RS)	Hospital de Clínicas de Porto Alegre da Universidade Federal do Rio Grande do Sul - UFRGS - HCPA	CAAE 57717516.3.2004.5327
Hospital Don Vicente Scherer (RS)	Irmandade Santa Casa de Misericórdia de Porto Alegre - ISCMPA	CAAE 57717516.3.2010.5335
Hospital Mãe de Deus (RS)	Hospital Mãe de Deus - Associação Educadora São Carlos - AESC	CAAE 57717516.3.2019.5328
Hospital Montenegro (RS)	Hospital Moinhos de Vento - HMV	CAAE 57717516.3.2003.5330

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Hospital São Lucas da PUCRS (RS)	Pontifícia Universidade Católica do Rio Grande do Sul - PUCRS	CAAE 57717516.3.2015.5336
Hospital Santa Cruz (RS)	UNISC - Universidade de Santa Cruz do Sul	CAAE 57717516.3.2002.5343
Hospital Santa Rita (RS)	Irmandade Santa Casa de Misericórdia de Porto Alegre - ISCMPA	CAAE 57717516.3.2010.5335
Hospital Tacchini (RS)	Associação Dr. Bartholomeu Tacchini - Hospital Tacchini /RS	CAAE 57717516.3.2032.5305
Pavilhão Pereira Filho (RS)	Irmandade Santa Casa de Misericórdia de Porto Alegre - ISCMPA	CAAE 57717516.3.2010.5335
Hospital Dona Helena (SC)	Hospital Moinhos de Vento - HMV	CAAE 57717516.3.2031.5330
Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto (SP)	Hospital das Clínicas da Faculdade de Medicina de Ribeirão Preto - USP	CAAE 57717516.3.2016.5440
Hospital do Coração (SP)	Hospital do Coração - Associação do Sanatório Sírio - Hcor	CAAE 57717516.3.2044.0060

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SPIRIT

STANDARD PROTOCOL ITEMS: RECOMMENDATIONS FOR INTERVENTIONAL TRIALS

SPIRIT 2013 Checklist: **Study protocol to assess the effectiveness and safety of a flexible family visitation model in adult intensive care units: a cluster-randomized, crossover trial (ICU VISITS STUDY)**

Section/item	Item No	Description	Addressed on page number
Administrative information			
Title	1	Descriptive title identifying the study design, population, interventions, and, if applicable, trial acronym	1
Trial registration	2a	Trial identifier and registry name. If not yet registered, name of intended registry	7, 12
	2b	All items from the World Health Organization Trial Registration Data Set	Supplemental file 1
Protocol version	3	Date and version identifier	25
Funding	4	Sources and types of financial, material, and other support	27
Roles and responsibilities	5a	Names, affiliations, and roles of protocol contributors	1-4, 26, 27
	5b	Name and contact information for the trial sponsor	27
	5c	Role of study sponsor and funders, if any, in study design; collection, management, analysis, and interpretation of data; writing of the report; and the decision to submit the report for publication, including whether they will have ultimate authority over any of these activities	28
	5d	Composition, roles, and responsibilities of the coordinating centre, steering committee, endpoint adjudication committee, data management team, and other individuals or groups overseeing the trial, if applicable (see Item 21a for data monitoring committee)	27

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Introduction			
Background and rationale	6a	Description of research question and justification for undertaking the trial, including summary of relevant studies (published and unpublished) examining benefits and harms for each intervention	9-11
	6b	Explanation for choice of comparators	9-11
Objectives	7	Specific objectives or hypotheses	11, 12
Trial design	8	Description of trial design including type of trial (eg, parallel group, crossover, factorial, single group), allocation ratio, and framework (eg, superiority, equivalence, noninferiority, exploratory)	12
Methods: Participants, interventions, and outcomes			
Study setting	9	Description of study settings (eg, community clinic, academic hospital) and list of countries where data will be collected. Reference to where list of study sites can be obtained	12, 13
Eligibility criteria	10	Inclusion and exclusion criteria for participants. If applicable, eligibility criteria for study centres and individuals who will perform the interventions (eg, surgeons, psychotherapists)	12-14
Interventions	11a	Interventions for each group with sufficient detail to allow replication, including how and when they will be administered	14-16
	11b	Criteria for discontinuing or modifying allocated interventions for a given trial participant (eg, drug dose change in response to harms, participant request, or improving/worsening disease)	15
	11c	Strategies to improve adherence to intervention protocols, and any procedures for monitoring adherence (eg, drug tablet return, laboratory tests)	19, 20
	11d	Relevant concomitant care and interventions that are permitted or prohibited during the trial	NA
Outcomes	12	Primary, secondary, and other outcomes, including the specific measurement variable (eg, systolic blood pressure), analysis metric (eg, change from baseline, final value, time to event), method of aggregation (eg, median, proportion), and time point for each outcome. Explanation of the clinical relevance of chosen efficacy and harm outcomes is strongly recommended	18-20
Participant timeline	13	Time schedule of enrolment, interventions (including any run-ins and washouts), assessments, and visits for participants. A schematic diagram is highly recommended (see Figure)	21,22

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Sample size	14	Estimated number of participants needed to achieve study objectives and how it was determined, including clinical and statistical assumptions supporting any sample size calculations	22, 23
Recruitment	15	Strategies for achieving adequate participant enrolment to reach target sample size	20-23
Methods: Assignment of interventions (for controlled trials)			
Allocation:			
Sequence generation	16a	Method of generating the allocation sequence (eg, computer-generated random numbers), and list of any factors for stratification. To reduce predictability of a random sequence, details of any planned restriction (eg, blocking) should be provided in a separate document that is unavailable to those who enrol participants or assign interventions	17, 18
Allocation concealment mechanism	16b	Mechanism of implementing the allocation sequence (eg, central telephone; sequentially numbered, opaque, sealed envelopes), describing any steps to conceal the sequence until interventions are assigned	18
Implementation	16c	Who will generate the allocation sequence, who will enrol participants, and who will assign participants to interventions	17, 18
Blinding (masking)	17a	Who will be blinded after assignment to interventions (eg, trial participants, care providers, outcome assessors, data analysts), and how	18
	17b	If blinded, circumstances under which unblinding is permissible, and procedure for revealing a participant's allocated intervention during the trial	NA
Methods: Data collection, management, and analysis			
Data collection methods	18a	Plans for assessment and collection of outcome, baseline, and other trial data, including any related processes to promote data quality (eg, duplicate measurements, training of assessors) and a description of study instruments (eg, questionnaires, laboratory tests) along with their reliability and validity, if known. Reference to where data collection forms can be found, if not in the protocol	18-22
	18b	Plans to promote participant retention and complete follow-up, including list of any outcome data to be collected for participants who discontinue or deviate from intervention protocols	12, 18-22

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Data management	19	Plans for data entry, coding, security, and storage, including any related processes to promote data quality (eg, double data entry; range checks for data values). Reference to where details of data management procedures can be found, if not in the protocol	18-22
Statistical methods	20a	Statistical methods for analysing primary and secondary outcomes. Reference to where other details of the statistical analysis plan can be found, if not in the protocol	23
	20b	Methods for any additional analyses (eg, subgroup and adjusted analyses)	23
	20c	Definition of analysis population relating to protocol non-adherence (eg, as randomised analysis), and any statistical methods to handle missing data (eg, multiple imputation)	12,22
Methods: Monitoring			
Data monitoring	21a	Composition of data monitoring committee (DMC); summary of its role and reporting structure; statement of whether it is independent from the sponsor and competing interests; and reference to where further details about its charter can be found, if not in the protocol. Alternatively, an explanation of why a DMC is not needed	22
	21b	Description of any interim analyses and stopping guidelines, including who will have access to these interim results and make the final decision to terminate the trial	NA
Harms	22	Plans for collecting, assessing, reporting, and managing solicited and spontaneously reported adverse events and other unintended effects of trial interventions or trial conduct	22
Auditing	23	Frequency and procedures for auditing trial conduct, if any, and whether the process will be independent from investigators and the sponsor	22
Ethics and dissemination			
Research ethics approval	24	Plans for seeking research ethics committee/institutional review board (REC/IRB) approval	25,26
Protocol amendments	25	Plans for communicating important protocol modifications (eg, changes to eligibility criteria, outcomes, analyses) to relevant parties (eg, investigators, REC/IRBs, trial participants, trial registries, journals, regulators)	25,26

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Consent or assent	26a	Who will obtain informed consent or assent from potential trial participants or authorised surrogates, and how (see Item 32)	26
	26b	Additional consent provisions for collection and use of participant data and biological specimens in ancillary studies, if applicable	NA
Confidentiality	27	How personal information about potential and enrolled participants will be collected, shared, and maintained in order to protect confidentiality before, during, and after the trial	26
Declaration of interests	28	Financial and other competing interests for principal investigators for the overall trial and each study site	28
Access to data	29	Statement of who will have access to the final trial dataset, and disclosure of contractual agreements that limit such access for investigators	26
Ancillary and post-trial care	30	Provisions, if any, for ancillary and post-trial care, and for compensation to those who suffer harm from trial participation	NA
Dissemination policy	31a	Plans for investigators and sponsor to communicate trial results to participants, healthcare professionals, the public, and other relevant groups (eg, via publication, reporting in results databases, or other data sharing arrangements), including any publication restrictions	26
	31b	Authorship eligibility guidelines and any intended use of professional writers	26, 27
	31c	Plans, if any, for granting public access to the full protocol, participant-level dataset, and statistical code	26
Appendices			
Informed consent materials	32	Model consent form and other related documentation given to participants and authorised surrogates	-
Biological specimens	33	Plans for collection, laboratory evaluation, and storage of biological specimens for genetic or molecular analysis in the current trial and for future use in ancillary studies, if applicable	NA

*It is strongly recommended that this checklist be read in conjunction with the SPIRIT 2013 Explanation & Elaboration for important clarification on the items. Amendments to the protocol should be tracked and dated. The SPIRIT checklist is copyrighted by the SPIRIT Group under the Creative Commons "Attribution-NonCommercial-NoDerivs 3.0 Unported" license.

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